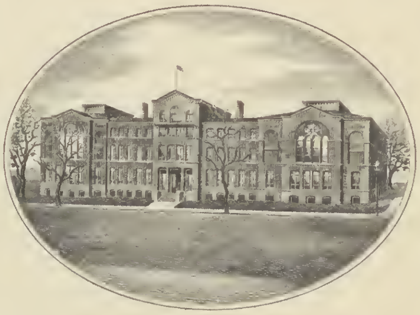
A BIBLIOGRAPHICAL SOURCEBOOK

OF

COMPRESSED AIR, DIVING AND SUBMARINE MEDICINE



A BIBLIOGRAPHICAL SOURCEBOOK
OF
COMPRESSED AIR, DIVING AND SUBMARINE MEDICINE

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PREFACE

THE publication of *A Bibliography of Aviation Medicine* (*3*) in 1942 and *A Bibliography of Aviation Medicine, Supplement* (*4*) in 1944 provided a source of reference to the literature in aviation medicine. The need has been felt for a similar compilation of the work in compressed air, diving, and submarine medicine. It has been suggested that such a volume would be more useful if it were to contain some indication of the contents of the references cited. An attempt to accomplish this has been made in the present Sourcebook. Each group of references is preceded by a review or summary of the literature quoted. Usually the contents of all the references in a particular subheading are summarized, but in some instances, papers have been included without specific discussion of them in the text. As far as possible, the findings and point of view of the investigators have been reported briefly and accurately and reference has been made to literature covering all sides of controversial issues. However, wherever trends of research and development can be clearly discerned, these have been indicated. It should be emphasized that this Sourcebook is not offered as a textbook of compressed air, diving, and submarine medicine, but is intended as an annotated guide to the existing literature in the field.

To give further information as to the contents of the papers cited, code letters have been inserted at the end of most entries in the bibliographical lists. *C* refers to classical or early reports. *P* indicates articles reporting experimental work contributory to progress in the particular subject. *M* is used to denote recent papers giving modern points of view. In regard to this code letter, it should be remembered that in certain rapidly developing aspects of compressed air, diving, and submarine medicine, no report can represent the current status of the problem for very long. *R* designates discussion or review papers. Reports with particularly useful bibliographies have been indicated with a *B*, while *Ch* is used to call attention to papers in which case histories are reported.

ARRANGEMENT AND STYLE

The classification, arrangement, and style follow the conventions observed in *A Bibliography of Aviation Medicine* and *A Bibliography of Aviation Medicine, Supplement.* References have been assembled according to the scheme of subject matter classification given below in the Table of Contents. Wherever unsigned articles are quoted, they are listed under "Anonymous" at the end of each subject group. Each entry has been assigned a serial number and the reference is cited by this number in the Index of Authors.

In all entries in the text and reference lists, surnames of authors are spelled as they appear in the original source. In books and theses, authors' names are given as they are printed on the original title page. In citing papers in journal literature, only the initials of given names are used and no attempt has been made to distinguish between male and female authors. It sometimes occurs, particularly in the French literature, that an author's surname appears without given names or initials. In citing such papers in the lists of references, the omission of initials is indicated by square brackets following or preceding the surname.

Titles of books and other separate publications are printed in italics, listing the full title, wherever possible, in the original language. If a translation is provided in the

original source, this is quoted in parentheses. In citing periodical literature, the title is given in full in roman type. The original language is used except in those languages requiring special alphabets. In such cases, if a translation into one of the commoner languages is supplied in the original article, this has been quoted in the citation in parentheses. Wherever a new translation has been made, this has been indicated by enclosing the translated title in square brackets. Whenever articles contain summaries in a second or third language, this information is given at the end of the citation.

In citing separate publications, the title is followed by the name of the city of publication, the publisher, the date and full pagination, all information following the title being set in roman type. In citing periodical literature, the journal abbreviation is given in italics followed by the date in roman type, the volume number in italics and the inclusive pagination in roman. If the volume of a particular journal is not continuously paged, the number within the volume is given in parentheses after the volume number.

A very few titles are included in the bibliographical lists which have not been checked from original sources. These have been marked with an asterisk.

All journals and handbooks from which references have been taken are cited in a separate list at the end of the Sourcebook. These items are arranged in alphabetical order of their abbreviations followed in each case by the full title. The system of abbreviations used conforms to *A World List of Scientific Periodicals published in the years 1900-1933, 2nd Edition.* For journals not included in the *World List*, abbreviations have been made up in conformity with *World List* conventions and such abbreviations are followed by an asterisk in the journal list but not in the lists of references. In preparing the journal list, the most recent city of publication of serials is given. Where a journal is no longer currently issued, the city from which it last appeared is quoted. No attempt has been made to indicate any relationship that may exist between serials of different titles. In cases where one journal has been amalgamated with another, or the title radically changed, separate abbreviations are listed.

In the Index of Authors, the names are listed in alphabetical order without distinction as to sole or joint authorship. In cases where variations of spelling of names exist, serial numbers are indexed under the commonest form of the name, with cross-references from the variant spellings.

ACKNOWLEDGMENTS

Special acknowledgment has already been made of the valued collaboration, assistance and encouragement of Captain E. W. Brown, (MC) U. S. Navy; Captain J. H. Korb, (MC) U. S. Navy; Captain C. W. Shilling, (MC) U. S. Navy; Captain A. R. Behnke, Jr., (MC) U. S. Navy; Captain T. L. Willmon, (MC) U. S. Navy; Lieutenant (jg) Dorothy M. Hain, H(W) U.S.N.R. and Phebe M. Hoff.

It is our privilege to acknowledge our very great indebtedness for help and criticism to members of the staffs of the U. S. Submarine Base, New London, Conn.; the Naval Medical Research Institute, National Naval Medical Center, Bethesda, Md.; and the Experimental Diving Unit, U. S. Navy Yard, Washington, D. C. We also desire to thank officers and men of submarines upon which trips have been made in the course of preparation of this Sourcebook.

We are particularly grateful to Captain O. W. Van Der Aue, (MC) U. S. Navy; Commander Ivan F. Duff, (MC) U.S.N.R.; and Lieutenant Commander Robert Hayter, (MC) U. S. Navy, for helpful suggestions in connection with certain portions of the manuscript and for calling to our attention references which had been overlooked.

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Most of the work of collecting and reviewing the literature included in this Sourcebook was carried out at the Army Medical Library, Washington, D. C. and we desire to record our indebtedness to Colonel Harold Wellington Jones and Colonel Leon L. Gardner for so generously making available the facilities of the library during a period of over a year and a half. We should like also to acknowledge with thanks the help of the staff of the Army Medical Library for their great assistance in handling and supplying the thousands of volumes which had to be consulted. Use has also been made of the facilities of the Library of the New York Academy of Medicine, New York and the Yale Medical Library, New Haven, Conn. and we should like to express our thanks to the staffs of both of these libraries.

We wish to record our very grateful thanks to Dorothy M. Immonen for her loyal and patient help in the arduous task of preparing the bibliographical citations. It is desired also to thank Harriet L. Johnson, PhM2c U.S.N.R. for technical assistance.

It is with pleasure that we acknowledge our indebtedness to Admiral H. W. Smith, (MC) U. S. Navy and Commodore J. C. Adams, (MC) U. S. Navy for their support and encouragement and particularly for their kindness in making available members of the secretarial staffs of the Research Division and the Division of Aviation Medicine in the preparation of the manuscript.

The task of preparing the manuscript for the press has required long hours of diligent effort and close attention to detail and we are particularly grateful to Alma M. Martin for her efficient cooperation in directing and participating in the final preparation of the manuscript. For their loyal and painstaking work on the manuscript, we should like to extend our sincere and grateful thanks to Florence B. Dunn, PhM3c U.S.N.R.; Helen F. Newman, S1c U.S.N.R.; Ruth C. Olson; and Anne F. Terzak, CY, U.S.N.R. We are also grateful for secretarial assistance given by Virginia Corn, PhM2c U.S.N.R.; Gladys N. Nisbett; Alice A. Shields; Lillian N. Smith, Y3c U.S.N.R.; and Frances E. White, CY, U.S.N.R.

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Although minute attention has been given to accuracy and completeness, errors and omissions will undoubtedly be found in this Sourcebook. For these we must assume entire responsibility and we shall be grateful to readers who use this volume if they will call our attention to them. The opinions or assertions contained herein are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

E. C. H.

Bureau of Medicine and Surgery,
U. S. Navy Department, Washington, D. C.
16 February 1948.

Table of Contents

History of the Medical Aspects of Submarines, Diving, and Subaqueous Tunneling

I. BIBLIOGRAPHIES

THE literature on compressed air, diving, and submarine medicine is widely scattered and most of it is to be found in journals and periodicals not specifically or exclusively devoted to this field. In fact, there is no journal of submarine medicine. A certain number of well-prepared bibliographical lists do exist, however, and one of the earliest of these is a collection of approximately 300 references which appeared in a monograph published in 1887 by Arntzenius (*2559*) on the therapeutic action of air under raised atmospheric pressure. While the literature quoted in Arntzenius' bibliographical list deals with a special aspect of compressed air, namely, its possible use as a curative agent, nevertheless, such literature is of importance in submarine medicine. In may cases, the same investigators were concerned with both the therapeutic and the industrial applications of compressed air and to some extent the work on the therapeutic use of air under pressure directly stimulated the development of the caisson. Paul Bert's classic work (*16*) published in 1878, and the large volume on caisson disease by Heller, Mager, and von Schrötter (*28*) which appeared in 1900, are both richly documented by references to the literature extant at the time. In 1907-08, von Schrötter also published a bibliographical review of the literature on caisson disease appearing subsequent to 1900.

Probably the most useful and complete bibliographies of caisson disease are to be found in two long review articles by Shilling (*1141*, *1142*) 1938 and 1941. These two papers are of particular value because of the care with which the literature has been reviewed and analyzed and the convenient way in which the references have been classified.

For technical literature on the subject of submarines as a whole, the reader is referred to a paper by Ellis (*1*) published in 1917, setting forth a list of references to material on torpedoes in the New York Public Library, and a similar list on submarines published by Jameson (*5*) in 1918.

Submarine medicine shares many important problems in common with other branches of naval medicine, particularly with the medical aspects of aviation. For this reason, the reader will find bibliographical source material on aviation medicine of value. This literature has been gathered together in four major bibliographies by Schmidt (*6*, *7*) 1938 and 1943-44, Hoff and Fulton (*3*) 1942 and Hoff, Hoff, and Fulton (*4*) 1944. Since submarine medical research laboratories have played such an important part in the advances in the military aspects of vision, particularly in recent years, the reader may wish to be familiar with modern research on this subject. The visual literature appearing between 1939 and 1944 has been compiled by Fulton, Hoff, and Perkins (*2*) 1945 under the auspices of the Committee on Aviation Medicine, Division of Medical Sciences, National Research Council, Washington, D. C.

1. **Ellis, W. A.** Torpedoes. A list of references to material in the New York public library. *Bull. N. Y. publ. Libr.*, 1917, *21:* 657–726. [B]

2. **Fulton, John F., Phebe M. Hoff, and Henrietta T. Perkins.** *A bibliography of visual literature 1939–1944.* Prepared for the Committee on Aviation Medicine, Division of Medical Sciences, National Research Council, acting for the Committee on Medical Research, Office of Scientific Research and Development, Washington, D. C. Menasha, Wis., George Banta Publishing Co., 1945, x, 114 pp. [B]

3. **Hoff, Ebbe Curtis and John Farquhar Fulton.** *A bibliography of aviation medicine.* Prepared for the Committee on Aviation Medicine, Division of Medical Sciences, National Research Council, acting for the Committee on Medical Research, Office of Scientific Research and Development, Washington, D. C. Springfield, Ill., Charles C. Thomas, 1942, 237 pp. [B]

4. **Hoff, Phebe Margaret, Ebbe Curtis Hoff, and John Farquhar Fulton.** *A bibliography of aviation medicine: supplement.* Committee on Aviation Medicine, Division of Medical Sciences, National Research Council, acting for the Committee on Medical Research, Office of Scientific Research and Development, Washington, D. C., 1944, xiv, 109 pp. [B]

5. **Jameson, M. E.** Submarines. A list of references in the New York Public Library (With a foreword to the list of references on submarines by Simon Lake.) *Bull. N. Y. publ. Libr.*, 1918, *22:* 17–69; 91–132. [B]

6. **Schmidt, Ingeborg.** *Bibliographie der Luftfahrtmedizin; eine Zusammenstellung von Arbeiten über Luftfahrtmedizin und Grenzgebiete bis Ende 1936.* Berlin, Julius Springer, 1938, 136 pp. [B]

7. **Schmidt, I.** Bibliographie der Luftfahrtmedizin. Zweite Folge. Eine Zusammenstellung von Arbeiten über Luftfahrtmedizin und Grenzgebiete 1937 bis Ende 1940. *Luftfahrtmed.*, 1943–44, *8:* 1–128 [B]

8. **Schrötter, H. von.** Verzeichnis der seit dem Jahre 1900 erschienenen Literatur über Kaisson- und Taucherkrankheit. *Hyg. Zbl.*, 1907–08, *3:* 397–403. [R, B]

II. GENERAL ARTICLES

In an official history of the medical aspects of World War II being prepared by the Bureau of Medicine and Surgery, Navy Department, sections will be devoted to medical problems of submarine operations and deep diving. This history, when it becomes available, should be consulted.

Readers wishing to familiarize themselves with the general aspects of compressed air medicine should not fail to acquaint themselves with the work of Paul Bert. For a complete list of Bert's publications cited in this Sourcebook, the index should be consulted. It is significant that Bert concerned himself with the physiological and pathological effects of both raised and reduced atmospheric pressures. This work was summarized by Bert (*16*) in his memorable volume published in 1878, and the reader is reminded that this book is now available in an English translation, prepared in 1943 by Hitchcock and Hitchcock. For a brief summarizing statement of Bert's work, his paper published in 1876 (*15*) may be read.

A study of compression and decompression on animals was reviewed by Philippon (*36*) in 1894 and 1895.

The lengthy monograph of Heller, Mager, and von Schrötter (*28*) published in 1900, is perhaps the most comprehensive work on compressed air physiology in the literature. Heller, Mager, and von Schrötter's book brings the subject up to the beginning of the 20th century and indicates the great strides made in knowledge of the symptomatology of raised atmospheric pressures and the management of caisson disease since the time of Paul Bert.

In 1906, there appeared a brief article by Carnot (*19*) which covers the whole field of pressure effects, including a description of Triger's caisson and the symptomatology and pathology of decompression sickness, together with a consideration of its treatment and prevention. Thomson's article (*40*) 1908 constitutes a technical description and discussion of caissons, together with rules for caisson workers. This author claimed to have worked at a pressure of 35 lb. per sq. in. for 86 hours, apparently entering and leaving the pressure chamber from time to time. During this period, he had two light attacks of the "bends." He did not, however, recommend such long periods of work and considered that caisson workers should not be exposed to pressure for more than 7½ hours at a time.

A comprehensive study on compressed air work and diving was published in 1909 by Boycott (*17*). This study is a handbook for engineers which includes deep-water diving and the use of compressed air for sinking caissons and for driving subaqueous tunnels. Boycott discussed selection of workers, ventilation, air supply and tables for compression,

hours of work, decompression, and recompression. Reference was also made to various types of diving dress, helmets, and diving bells. The author also referred to the use of caissons in bridge construction and to the technical aspects of underwater tunneling.

Two papers by Hill (*29*, *30*) published in 1911 and 1912, are considered of general interest. Mention may also be made of Hill's book on the subject, also published in 1912. Hill's paper (*30*) 1912 is of particular value for its illustrations showing pathological lesions produced by rapid decompression in the kidneys, heart, liver, mesentery, brain, and spinal cord. In 1915-16, Halliday (*26*) reviewed the available literature on deep sea diving and its relation to caisson disease. This paper includes a historical résumé of the development of diving and a consideration of the physics and physiology of subaqueous work.

For a more recent review article on deep sea diving, the reader may consult a paper by French (*22*) 1922. In Haldane's monograph on respiration (24) 1922, there is a chapter on the effects of high atmospheric pressures which not only reviews his own work but also includes a description of the diving dress and the development of the diving bell and the caisson. The reader will find a good review of Haldane's investigations for the Admiralty Committee on Deep Water Diving on the effects of excess carbon dioxide in the diver's helmet. The prevention of decompression sickness by Haldane's method of stage decompression is given in detail as well as the application of this method to diving and to tunneling. Oxygen poisoning is also discussed.

Attention is called to part VI in a series of papers by DuBois (*20*) 1929 on the physiology of respiration in relation to naval medical problems. DuBois has included an excellent history of diving and diving dress as well as a consideration of naked divers, the effects of compressed air and bubble formation and a review of the literature on caisson disease. In 1930, Hill (*31*) published a short commentary on diving which briefly summarizes the Davis submarine dress and the dangers to which divers are subjected. More recent work on deep sea diving was described in 1931-32 by Phillips (*37*) and by Hill and Phillips (*32*) in 1932. The latter paper may be consulted for a commentary on various theories of etiology of decompression sickness.

The particular hazards to which submarine personnel may be exposed were discussed in 1935 by Dudley (*21*). This paper deals with submarine escape accidents as well as the effects of hot atmospheres, excess carbon dioxide, poisoning with carbon monoxide, suffocation in sealed compartments, and the effects of smoke fumes and carbon tetrachloride. Also in 1935, there appeared a paper on the physiology of deep sea diving by Thomson (*41*) in which he considered carbon dioxide poisoning, oxygen poisoning, and compressed air illness in relation to divers. Decompression techniques and the use of the Davis submerged decompression chamber were described. The effect of breathing oxygen during decompression was also considered.

One of the most complete discussions and reviews of work in compressed air in industrial operations was published in 1936 by Singstad (*39*). This report is frequently referred to in this Sourcebook and should be read by all those concerned with the problems of raised atmospheric pressure in industry. For a similarly comprehensive and yet brief review of the dangers to which divers are exposed, reference may be made to a paper published by von Mauntz (*35*) in 1937. This article includes a description of the symptomatology, etiology, and pathology of caisson disease as observed in divers; consideration is also given to the subject of prophylaxis and therapy of caisson disease. The author also describes diver's "squeeze." The paper contains a useful bibliography.

In 1938, Behnke (*10*) discussed problems which arise in connection with submarine personnel. Behnke stressed the importance of selection and of training, and emphasized the need for adequate medical facilities aboard tenders and at bases. Various research problems of importance in submarine medicine were raised. For a general discussion of the submarine service of the United States Navy, the reader may consult a paper by Harrison (*27*) 1938. Harrison called attention to John

P. Holland's launching of his first submarine boat in 1875. The early Holland boats operate practically awash when in the surface position and in this position had 6 percent reserve buoyancy. Later boats of the "submersible" type had a reserve buoyancy of 30 to 40 percent and were capable of more rapid and steeper dives. The modern submarine has both features: (a) "level keel" and (b) the reserve buoyancy submerging principle. The Holland Boat No. 9 (the *Holland*) built and tested in 1898–1900, was the first craft combining these two principles and served as a model for American and British submarines. Harrison's article is of further interest because it contains a complete list of United States and foreign submarine disasters between the years 1902 to 1915 and 1921 to 1936.

In 1939, Behnke (*11*) reviewed current medical problems relating to diving, underwater construction, and submarines. The paper included a consideration of changes in barometric pressure as they affect the auditory mechanism and a discussion of the patency of the Eustachian tubes and the nature of nitrogen narcosis (compressed air intoxication). The problem of avoiding dangerously high percentages of carbon dioxide in diver's helmets was also discussed as well as the poisonous action of oxygen and the effect of carbon dioxide in rendering both nitrogen and oxygen more toxic at high pressures. In 1942, Behnke (*12, 13*) also published a general review covering the subjects of deep diving as well as high altitude flying, discussing aeroembolism and its prevention by pre-oxygenation and by step-wise decompression. The use of helium, the etiology of the "bends" and tests for selection of personnel were also discussed. An excellent review of the physiological effects of gases at high pressure, particularly in relation to deep diving and the submarine service, was published in 1942 by Behnke and Stephenson (*14*). This long and comprehensive review is well documented by bibliographical references to the literature.

In a general article on the medical problems of diving and submarines, Johnson (*34*) in 1940 discussed selection of submarine personnel, dangers of low oxygen and excess carbon dioxide, ventilation, rescue apparatus, caisson disease, the use of the recompression chamber, and submarine rescue. Selection and training of submarine personnel was discussed by Shilling (*38*) in a paper on medical problems in submarine warfare published in 1945.

Readers will find helpful allusions to problems related to submarine and compressed air medicine in Burns' *Introduction to Biophysics* (*18*) 1921 and Armstrong's book on aviation medicine (*9*) which appeared in 1943.

9. Armstrong, Harry G. *Principles and practice of aviation medicine.* Second edition. Baltimore, Williams and Wilkins Company, 1943, xiv, 514 pp.

10. Behnke, A. R. Submarine medicine. *Milit. Surg.*, 1938, *83:* 6–19. [M, R]

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13. Behnke, A. R., Jr. Investigations concerned with problems of high altitude flying and deep diving; application of certain findings pertaining to physical fitness to the general military service. Pp. 406–429 in: *War medicine: a symposium.* Edited by Winfield Scott Pugh. New York, Philosophical Library, 1942, 565 pp. [M, R]

14. Behnke, A. R. and C. S. Stephenson. Applied physiology. *Annu. Rev. Physiol.*, 1942, *4:* 575–598. [M, R]

15. Bert, P. La pression de l'air et les êtres vivants. *Rev. sci., Paris*, 1876, Ser. 2, *11:* 49–55. [C]

16. Bert, Paul. *La pression barométrique; recherches de physiologie expérimentale.* Paris, G. Masson, 1878, viii, 1168 pp. [English trans. *Barometric pressure. Researches in experimental physiology.* Translated from the French by May Alice Hitchcock and Fred A. Hitchcock. Columbus, Ohio. College Book Company. 1943, xxxii, 1055 pp.] [C, P, B, R]

17. Boycott, George Walter Morgan. *Compressed air work and diving. A handbook for engineers comprising deep water diving and the use of compressed air for sinking caissons and cylinders and for driving sub-aqueous tunnels.* London, C. Lockwood and son, 1909, xii, 116 pp.

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21. Dudley, S. F. Some atmospheric hazards encountered in naval life. *Proc. R. Soc. Med.*, 1935, *28* (Unit. Serv. Sect.): 1283–1292. [R]

22. French, G. R. W. Remarks on deep-sea diving. *Nav. med. Bull., Wash.*, 1922, *17:* 701–722 [R]

23. Galligo, J. S. Higiene y patología del submarino. *Clín. mod.*, 1915, *14:* 210–213; 225–229.

24. Haldane, J. S. *Respiration.* New Haven, Yale University Press, 1922, xviii, 427 pp. [R]

25. Haldane, J. S. and J. G. Priestley. *Respiration.* New Haven, Yale University Press, 1935, xiii, 493 pp. [R]

26. Halliday, C. H. Deep sea diving and its relation to caisson disease. Being an abstract of the available literature. *Amer. J. trop. Dis.*, 1915–16, *3:* 502–512. [B, R]

27. Harrison, W. C. United States navy submarine service. *Nav. med. Bull., Wash.*, 1938, *36:* 277–306. [R]

28. Heller, R., W. Mager, and [ ] v. Schrötter. *Luftdruckerkrankungen mit besonderer Berücksichtigung der Sogenannten Caissonkrankheit*, Wien, Alfred Hölder, 1900, ix, 1230 pp. [P, R, Ch]

29. Hill, L. The physiology of submarine work. *Rep. Brit. Ass.*, 1911, *80:* 634–647. [P]

30. Hill, L. E. Compressed air illness and experimental research. *Brit. med. J.*, 1912, *1:* 348–353. [P]

31. Hill, L. Diving. *Nature, Lond.*, 1930, *125:* 415–417. [R]

32. Hill, L. and A. E. Phillips. Deep-sea diving. *J. R. nav. med. Serv.*, 1932, *18:* 155–173. [R]

33. Hosmer, H. R. Submarines in periodical literature from 1911 to 1917. *J. Franklin Inst.*, 1917, *184:* 251–306. [B]

34. Johnson, L. W. Medical problems of diving and submarines. *N. Y. St. J. Med.*, 1940, *40:* 1065–1074. [M, R]

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37. Phillips, A. E. Recent research work in deep sea diving. *Proc. R. Soc. Med.*, 1931–32, *25:* 693–703. [R]

38. Shilling, C. W. Medical problems of submarine warfare. *Milit. Surg.*, 1945, *96:* 223–226. [M, R]

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39. Singstad, O. Industrial operations in compressed air. *J. industr. Hyg.*, 1936, *18:* 497–523. [M, R]

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41. Thomson, W. A. R. The physiology of deep-sea diving. *Brit. med. J.*, 1935, *2:* 208–210.

42. U. S. Navy. Bureau of ships. *Diving manual 1943.* Washington, D. C. Govt. print. off., 1943, 267 pp.

43. U. S. Navy. Bureau of medicine and surgery. *Manual of the medical department, United States Navy.* NavMed–117 (rev. 1945), Washington, D. C. Govt. print. off., 1945, 605 pp.

III. HISTORY OF DIVING

For a complete review of the history of deep diving and underwater rescue, the reader is referred to three long articles by Davis (*48, 49, 50*) published as the *Thomas Gray Lectures* in 1934. A similarly lucid account, dealing with the development of diving apparatus, has been given in a paper published by Singstad in 1936 (*39*).

Davis called attention to certain interesting adaptations of diving animals: The whipped-tailed larva, *Erstalis tenax*, possesses a tail capable of extending up to a length of 6 inches and containing a pair of air tubes opening at the top in a star-shaped flange which floats on the surface of the water. Through these tubes, the larva sucks in air. A similar adaptation is to be found in the grub of a certain beetle (*Donacia*) which is equipped with a pair of slender, curved spines at the end of the body which the animal inserts into the air-filled tubes of water plants. The water spider has an adaptation similar to a diving bell with which it is able to provide air for itself while submerged. This spider spins a case or cocoon which it fills with bubbles of air trapped on the hairs of the hinder parts of the body.

These adaptions recall attempts made by human beings in times past to survive in a subaqueous environment. As will be seen, man has tried for centuries to penetrate the depths of the sea, and the limitations of diving without equipment have stimulated him to create more and more elaborate methods of supplying respirable air under water. However, much useful underwater activity has been

carried out by naked divers without any equipment whatever and these individuals have developed remarkable capacities for remaining below the surface. According to Davis (*48*) 1934, an English professional swimmer, Finney, remained below the surface in a tank of warm water for 4 minutes 29¼ seconds in 1886. During the time of submergence, the diver did no work whatever. In 1893, Beaumont, an Australian, stayed under water for 4 minutes 35 seconds and an American named Enoch was reported by Davis as having remained under water continuously for 4 minutes 46¼ seconds. Naked sponge divers operating without apparatus do not usually remain below surface for more than 1½ minutes at a time, nor do they customarily dive to depths greater than 80 to 100 ft. Cases of bleeding from the nose, ears, and mouth are quite common and sometimes divers are brought up insensible. Davis reports that Stotti Georghios, a Greek sponge diver, in 1913 stayed under on several occasions for 1 minute and 30 seconds to 3 minutes and 35 seconds at depths of 130 to 200 ft. in recovering an anchor and chain belonging to the Italian battleship, *Regina Margharita*, which was lost at a depth of about 200 ft. in the bay of Pegodia.

de Méricourt (*54*) 1869 reported that sponge divers frequently dived to depths of 45 to 55 m. and remained on the bottom for 2 to 4 minutes at a time. These divers were reported as having made five to six such dives per day. Frequently, they had hemorrhages from the eyes, nose, and mouth after surfacing. French divers using a simple diving dress suffered no fatalities, but naked divers were frequently paralyzed and died as a result of the dives. Petechial hemorrhages of the skin and mucous membranes, noted in these divers, were ascribed by de Méricourt to too rapid decompression. This author laid down rules for divers wearing diving suits; in particular, he considered that at 30 m., the duration of work at the bottom should be restricted to 2 hours. He believed that descent should be as rapid as equilibration of the ears permits and that decompression should be slow and governed by the depth of the dive. The decompression rate recommended by divers with equipment was 1 minute per meter of depth.

In 1881, Parissis and Tetzis (*57*) discussed the medical problems of sponge divers of the Island of Hydra in Greece. Over a period of 30 years, as a medical practitioner, Tetzis observed these sponge divers in health and disease. These individuals used a special dress and there were many cases of pain, paraplegia, local anesthesia, disturbance of bladder function, etc. on decompression. The monograph by Parissis and Tetzis contains a number of detailed case histories. Autopsies on fatal cases revealed hemorrhages in the spinal cord.

The medical problems of naked divers was discussed in 1887 and 1887-88 by Lacassagne (*53*) who spoke of divers in India who were able to remain under water for 10 to 15 minutes. The author himself stated that sponge and pearl fishers in the Mediterranean Sea and the Indian Ocean remained submerged for no longer than 10 minutes. He records that a diver in artesian wells in Algeria was able to hold his breath for no longer than 2 minutes 33 seconds. A certain "Miss Lurine" held the breath for 2½ minutes and James, a Hungarian, was quoted as having remained submerged for 4 minutes 40 seconds in England in 1885. This individual was reported as having swum under water a distance of 150 m. in 4 minutes. According to Barbe (*44*) 1900 spasmodic paraplegia in sponge fishers characterized by anesthesia and hyperesthesia of the limbs, muscle spasms or convulsions, incontinence or retention of urine, and paralysis, was caused by too sudden release of gases, principally nitrogen, dissolved in the blood under high pressure. Musenga (*55*) 1915 recorded that naked sponge fishers dived to depths of 80 m. without apparatus. The techniques of holding the breath in naked diving without apparatus were described in 1921 by Thooris (*59*).

One of the most interesting aspects of diving without apparatus is provided by the Japanese female divers, the so-called "Amas."

These women wear no equipment except goggles for the eyes and a weight to help them submerge. The husband assists from the boat but does not dive himself. The profession of women divers in Japan has arisen from an idea long prevalent in that country that the cold water was harmful to the testicles in the male and produced sterility. Some of these women divers were reported by Teruoka (*58*) 1931-32 as having descended to depths of 45 m. and in a case recorded, a depth of 30 m. was attained. The "Ama" remains below the surface for about 2½ minutes and carries out as many as 20 dives an hour and about 60 to 90 dives a day. Between each 2 hours' work, there is a pause for rest of about 1½ hours. One "hour's" work is referred to as *Kakura* and the duration of an "hour's" work or a Kakura varies, according to the temperature of the water between 30 and 70 minutes. These divers do not suffer from caisson disease since the time of compression is so short.

Many classical illusions to diving may be found recorded in Davis' review (*48*). In particular, naked divers were used by Xerxes and by many others to recover sunken treasure or in battle to destroy harbor defenses or to cut ships' cables. Plutarch records an extraordinary story of a fishing contest by Anthony and Cleopatra in which Anthony hired divers to put fish on his own line. It appears that Cleopatra discovered his fraud and hired a rival diver to put a salt fish on his line, doubtless to his great consternation and embarrassment.

Diving appliances were suggested from very early times, and according to Davis, Pliny in 77 A.D. refers to divers employed in warfare who drew in air through a tube, one end of which was held in the mouth and the other end was supposed to have floated on the surface. Pliny compared this to the practice of elephants who breathed through the trunk while remaining submerged. As is well known, however, such a device will work only in a few feet of water since a differential of pressure between the outside of the body and the inside of the lungs created by any greater depth would render breathing impossible and lead to hemorrhage in the respiratory system. In about 1500, Leonardo da Vinci designed several diving appliances, none of which was probably ever constructed. Davis illustrated one such suit in which the helmet was connected to the surface by means of a flexible pipe. This suit would never have functioned. A suit based on the same principle is illustrated, according to Davis, in an edition of a treatise on warfare by Flavius Vegetius Renatus published in 1511. This appliance was a complete suit provided with a leather helmet communicating with the surface by a slender tube, the upper end being supported by a float. Bonajuta Lorini in 1597 was reported by Davis to have published a description of a similar apparatus with a large-bore pipe connected to the helmet.

Several early workers described self-contained diving apparatus. For example, Borelli in 1680 described a system with a leather dress and a metal helmet. The air in the helmet was circulated through a curved metal pipe where it was cooled and this was supposed to purify it, so that it could be breathed again. Klingert, in 1797, designed a complete diving dress with a large helmet connected to the surface by twin breathing pipes. No provision was made for compressing the air delivered to the helmet and hence the apparatus was unsuitable for diving. Klingert also designed a large air reservoir which was cylindrical in shape with conical ends and provided with a platform on which the diver stood. The diver breathed in through an intake pipe at the top and exhaled through an outlet pipe at the bottom. The cylinder was provided with a piston and tube worked by the diver, so that he could rise and submerge by himself. Unfortunately, there is no information as to whether this apparatus was ever used.

The history of modern diving dress begins with the introduction in 1819 by Augustus Siebe (*49*) of the original "open" diving dress which consisted of a metal helmet riveted to a waterproof flexible jacket reaching to the diver's waist. Air under pressure was pumped into the helmet and escaped through the lower part of the jacket. With this appliance,

divers could actually descend under water and remain for considerable periods of time. There was danger of filling the jacket and helmet with water if the diver bent over carelessly However, good work was done with this suit and a great deal of the dispersing of the wreck of the *Royal George* sunk off Spithead in 1784 was carried out by divers wearing the open suit. In 1837, Siebe introduced the "closed" dress, in which the helmet was secured to the suit by a watertight connection and which was also watertight at the wrists and feet. Air was supplied under pressure through a non-return valve at the back of the helmet by means of a flexible tube connected with an air pump. Air escaped through an adjustable valve at the side of the helmet. Thus, the pressure in the helmet was always equal to or slightly greater than the water pressure at the outlet valve. The suit was provided with lead weights at the chest and back and on each boot.

In 1825, William H. James designed a self-contained diving dress provided with a supply of compressed air from an iron reservoir in the form of a cylindrical belt. In 1842, Sandala, a Frenchman, suggested a self-contained regenerative system dress which, however, was never constructed. The first practicable design for a self-contained dress was worked out in 1878 by H. H. Fleuss in association with Siebe, Gorman and Company. This suit was provided with a copper chamber containing caustic potash for absorbing carbon dioxide. Below this chamber, there was a cylinder of oxygen under a pressure of 450 lb. per sq. in. With this apparatus, Alexander Lambert entered the flooded Severn Tunnel in 1882 and closed a large valve under a pressure provided by a 40-foot head of water.

The diving suits considered above were made of flexible material and the pressure to which the body of the diver was subjected depended upon the depth at which he was operating. It early became apparent that there were limits to the depths to which a diver could descend with such equipment. For example, van Musschenbroek (*56*) 1739 stated that divers could descend in a diving bell to depths as great as 300 ft. below the surface but that it was necessary to renew the condensed air continually. It is of interest that van Musschenbroek also carried out experiments on decompression of animals to pressures below one atmosphere. He noted that animals died if the atmosphere was sufficiently decompressed and made the shrewd observation that fetuses had a greater tolerance to decompression than grown animals. van Musschenbroek ascribed this to the fact that fetuses live without breathing through the lungs. As is well known from modern experimental work, fetuses and newborn animals show a much greater tolerance to anoxia than adult animals of the same species.

One of the earliest attempts to build a rigid armored diving dress which would permit the diver to descend below the surface and at the same time remain in an environment maintained at a pressure of one atmosphere was carried out by Lethbridge in Devonshire in 1715. This device was a kind of watertight barrel with holes for the arms and a glass window for observation and was used with some success.

In 1838, Taylor constructed an all-metal diving suit provided with articulated joints similar to a flexible metal voice pipe. Philips (*49*) in 1856 designed a suit in which the body was enclosed in a short, thick metal cylinder, domed at the ends with ball-and-socket joints at the arms and legs. The arms terminated in nippers. In 1913, Neufeldt and Kuhnke and Company (*49*) constructed an armored dress with ball-and-socket joints provided with ball bearings, and in 1920 the same firm made a much improved dress which incorporated a self-contained oxygen supply and a carbon dioxide absorbent. The suit was surmounted by a circular ballast tank which could be flooded or "blown" at will. The Peress armored suit differs from the Neufeldt and Kuhnke apparatus mainly in the type of joints. The Peress joints were sealed with a liquid trapped between the metal parts. The suit weighs 800 lb. and there are no buoyancy trimming tanks. A telephone and regenerative breathing apparatus are provided.

The history of diving bells goes back to references by Aristotle to the use of such bells by Alexander the Great, at the seige of Tyre in approximately 332 B.C. Davis (*49*) quoted several other early allusions to the use of diving bells. In particular, two Greek divers exhibited a diving bell before Emperor Charles V in Toledo in 1538. Bells were used by a number of individuals to retrieve sunken treasure. Davis referred to William Phipps, one of the world's most famous treasure seekers, who in 1680 retrieved £200,000 with a diving bell. Up to this time, there were no provisions for adequately renewing the air within the bell but in 1690, Edmund Halley (*49*), Secretary of the Royal Society, designed and constructed what was undoubtedly the forerunner of the modern diving bell. This device was constructed of wood and had a cubic capacity of 60 cu. ft., being 3 ft. in diameter at the top. The bell was coated with lead sheeting and was provided with clear, strong glass set into the top. Fresh air was supplied to the bell when submerged from two lead-lined barrels each having a bung-hole at the top and at the bottom and a leather tube through which air could be forced from the barrel to the bell by tilting up the barrel. The barrels could be hauled to the top to renew the air as required. In this bell, Halley remained at a depth of 10 fathoms for 1½ hours.

In 1788, John Smeaton (*49*) designed the first modern diving bell for use in repairing the foundations of Hexham Bridge in England. There was a force pump on the roof of the bell which provided the occupants with a continuous supply of fresh air under pressure. The top of the bell was not submerged so that the device was really a form of movable caisson. Siebe, Gorman and Company (*49*) constructed many types of diving bells. One of these was built for the British Admiralty to lay and repair moorings at Gibraltar. This bell was installed on a carrier vessel and was provided with a lock through which entry and exit could be effected. It appears that decompression symptoms were not frequently encountered by personnel descending in diving bells and the early literature contains no clear account of such symptoms. Colladon (*47*) 1826 who made descents to a depth of 30 ft. in a diving bell at Howth near Dublin did not refer specifically to symptoms of caisson disease although he remained at depth for 1 hour. He did, however, report pains in the ear and difficulty of hearing on descent and mentioned attacks of colic and headaches.

Submersible observation chambers have played a significant role in underwater activity and Davis (*50*) designed such a chamber in 1921. In 1930, Beebe constructed a spherical chamber in which he and Barton (*2139*) descended to a depth of 1,426 ft. off Bermuda. The chamber was a spherical steel casting weighing 5,000 lb. It was 4 ft. 9 in. in diameter and the walls were 1½ in. thick. There were three observation windows made of fused quartz 8 in. in diameter and 3 in. thick. Oxygen was provided for two persons for about 6 hours and soda lime and calcium chloride were used to absorb carbon dioxide and moisture. The cable was tested up to 29 tons and the chamber was provided with electric light and telephone.

Of the medical and physiological research leading up to modern systems of deep diving, a few brief comments may be made. The early work of investigators interested in the effects of air under pressure in the treatment of disease undoubtedly stimulated studies of the actions on the body of the higher pressures to which diving operations subjected human beings. Paul Bert unified and advanced this knowledge in great measure. Through his investigations, and the observations of others, it became clear that decompression symptoms might be prevented or minimized by slow, gradual decompression. The danger of high percentages of carbon dioxide in the air breathed by the diver also began to be recognized and in 1893, Moir (*1112*) installed the first recompression chamber for treatment of the "bends" at the Hudson River operations. In 1906, the British Admiralty appointed a deep diving committee on which Haldane was the physiological member. Haldane came to the conclusion that when the excess of atmospheric pressure does not exceed 1¼

atmospheres, there is immunity from symptoms due to decompression however long the exposure to compressed air or however rapid the decompression. Bubbles are not formed, according to Haldane, unless the supersaturation corresponds to a decompression from more than a total pressure of 2½ atmospheres. The volume of nitrogen liberated is the same when the total pressure is halved whether the pressure be high or low. Hence, it is just as safe, according to Haldane, to go rapidly from 4 atmospheres to 2, or from 6 atmospheres to 3 as from 2 atmospheres to one. As a result of his investigations, Haldane recommended the "stage" method of decompression which was adopted by the committee in 1907 and for which the Admiralty set 210 ft. as the limit of diving operations. (See Henderson (*67*) 1936.)

Davis concluded his third article (*50*) 1934 by reference to the submersible decompression chamber. This chamber is let down into the water and the diver enters it from a hatch beneath. This hatch is then closed and the chamber can be raised to the surface and decompressed at any desired rate. Using this chamber, divers can be decompressed in a warm, dry environment. With this apparatus, men have worked safely at a depth of over 300 ft.

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IV. HISTORY OF CAISSON AND TUNNELING OPERATIONS

For comprehensive reviews of the history of underwater industrial operations, the reader is referred to Singstad's article (*39*) published in 1936 and a monograph by Smith (*76*) which appeared in 1873. It seems probable, according to Smith, that the work of Junod, Tabarié, Pravaz, and others on the therapeutic use of compressed air chambers first suggested the employment of compressed air as a substitute for pumping out the water in subaqueous mining operations. The work of these investigators and others is reviewed in the section on the therapeutic effects of gases under raised atmospheric pressures (p.302). Singstad (*39*) 1936 called attention to the fact that Cochrane conceived and patented

the idea of using compressed air in shaft and tunnel work in water-bearing ground. With his proposed apparatus for compressing atmospheric air within subterranean excavations, Cochrane hoped to obviate the dangers due to leakage of water into the excavation. His proposal included the use of an air lock to permit the passage of men and material without loss of air pressure inside. Cochrane's scheme was apparently never carried into operation.

In 1841, Triger (*77*) reported on the use of the first caisson designed by him for penetrating the quicksands in the bed of the Loire River near Chalonnes in France. This caisson was constructed of iron cylinders 1.033 m. in diameter, each section being about 5 to 6 m. long. The caisson was sunk to a depth of 20 m. and the air in the caisson was compressed to a pressure corresponding to the pressure head of water by means of a pump at the surface. At the top, a lock was provided through which the men could pass. In his first report, Triger described pain in the ears during the period of compression. Pain ceased when the men were fully "locked in." At 3 atmospheres (absolute), candles burned much more rapidly. The air was warmed during compression and workers had a feeling of chilliness during the period of decompression. It was impossible to whistle at 3 atmospheres and the voice had a nasal sound. The rate of respiration was said to be reduced. Laborers claimed that when ascending the ladder from the working chamber while still under pressure, they felt much less out of breath than when performing similar exertion in the open air. One of the workers who had been deaf since the seige of Antwerp in 1832 asserted that he always heard more distinctly in the compressed air than did his comrades.

Two laborers, after working for 7 hours in the chamber, experienced severe pains—one in the left arm and the other in the knees and left shoulder—one-half hour after emerging into the open air. The pains were relieved by rubbing the affected region with alcohol and both workmen returned to work the next day. These are the first recorded cases of caisson disease. In 1845, Triger (*78*) reported on the effect of compressed air on the health of workers and again called attention to painful ear symptoms during compression. Swallowing alleviated this pain and Triger understood that this was due to the fact that air entered the middle ear via the Eustachian tube and thus equalized the middle ear pressure. Triger's paper also contains a report of the two cases of caisson disease previously referred to. Triger's observations on the effect of compressed air on his workmen were again reported in a brief paper (*79*) published in 1845. He again referred to pain in the ears on compression and noted that alcoholic intoxication tended to make the pain worse. Triger was interested in the effects of high pressure on sounds and took a violin into the caisson and played it. He stated that the sound appeared to lose about half of its intensity at 3 atmospheres (absolute). He also kept a dog and a bird in the caisson for many days in succession without harm to either animal. Triger envisaged the use of his system of compressed air in sinking caissons for bridges, in retrieving valuable objects from river beds and in driving tunnels through water-bearing ground. In a further report published in 1845, Triger (*80*) described the effects of explosion of blasting powder in caissons at 3 atmospheres. It appeared to him that the shock of the explosion was stronger than under normal pressure. In 1852, Triger (*81*) was awarded the *Prix de mechanique* for his invention of the caisson. For further descriptions and reference to Triger's caisson, the reader should consult two papers published in 1843 by Detmold (*64*) and in 1857 by Fleury (*65*).

In 1846, Blavier (*63*) described the use of the caisson at the Douchy mines (Nord) in France. Using a 14-horsepower steam engine to operate the compression pumps, it was possible to penetrate to a depth of 20 m. Blavier's article contains a description of the construction and operation of his caisson and a discussion of the physiological effects of compression and decompression on the workers. Reference was also made to the pain in the ears which ceases when the maximum pressure is reached. The author remained in the caisson

for 2 hours without symptoms and laborers worked in the chamber consecutively for 6 hours without any untoward effects. It was claimed that there was greater difficulty in breathing under pressure than in free air but this apparently did not manifest itself except as a feeling of relief on leaving the lock. No change was found in the pulse rate after 1 hour at a pressure of 2.6 atmospheres (absolute). On decompression, the chamber was filled with dense fog and there was a feeling of cold. Blavier believed that only young, healthy individuals should be allowed to engage in caisson work. Many workers at Douchy, even though healthy, frequently experienced a feeling of heaviness in the head and pains in the limbs for some hours after leaving the caisson. One of the workers was stricken with a complete paralysis of the arms and legs for 12 hours after leaving the caisson. The pains following decompression yielded to local massage. Although Blavier had no symptoms during his first visit in the working chamber under pressure, he did experience pains in the left side for several days beginning the day after the visit. Thinking that the cause of the pains was the cold, Blavier re-entered the caisson later, taking precautions against cold. Even so, after leaving the chamber, pains were experienced which persisted for some 4 to 5 days.

As will be seen by a survey of Smith's paper (*76*) 1873 and the report by Singstad (*39*) 1936, the pneumatic method was rapidly adopted in the construction of the foundations of bridges. The medical aspects of one of these construction operations, namely the building of the foundations of a new bridge across the Medway at Rochester in England, was described in 1850-51 by Hughes (*68*). This bridge was constructed on the site of an old bridge that had been built about 1115 A.D. At first, an attempt was made to force cylindrical piles into the ground by the so-called pneumatic method of Potts which had been successfully tried out in other places. This was a suction method to keep the water sucked out of the working chamber. The technique was found, however, to be inadequate under the conditions prevailing at the Medway operations. It was therefore decided to use an air-compression method, that is to say, a plenum rather than a vacuum system so as to give each pile the character of a diving bell. The cylinders which were used in constructing the caisson were 7 ft. in diameter and 9 ft. long and two air locks were provided. The compression pumps were driven by 6-horsepower, noncondensing steam engines. Hughes continued his article by describing earlier diving bells and construction work carried out with them. The original caisson built by Triger was also described. In the men employed in the Medway operations, Hughes noticed pain in the ears on compression which was relieved by swallowing. He also reported greater facility in hearing, augmented appetite, slight changes in respiratory rate and depth, and more rapid combustion of candles.

Although the pathological symptoms following decompression were observed from the very beginning of caisson operations, it was not until the report of Pol and Watelle (*75*) in 1854, that a serious scientific study was made of the effects of raised atmospheric pressure and decompression upon the human body. A description was given by Pol and Watelle of the sinking of a shaft at Lourches. In an explosion of a caisson at a pressure of 3.7 atmospheres (absolute), six lives were lost. Pol and Watelle described symptoms of compression and of work at high pressures. On decompression, there was an increase in the pulse rate and there were several cases of untoward symptoms among workers. Some laborers reported muscular pains and in some cases there were convulsions and unconsciousness. In addition to the six who died in the explosion, one worker died as a result of decompression. This individual had been suffering with cramps and weakness and entered the pressurized chamber without authorization. He worked for 1 day and died shortly after decompression. At autopsy, the meninges were found injected and the sinuses filled with blood. The heart was enlarged and the bronchi congested with bloody mucus. The stomach was distended and its walls were hyperemic. Pol and Watelle

concluded that pressures up to 4.25 atmospheres (absolute) can be withstood safely. The danger of accidents increases with increasing pressure. The lesions indicated pulmonary and cerebral congestion. Workers between the ages of 18 and 26 were stated to be most tolerant of high pressures. Pol and Watelle believed that the harmful effects of pressure were due to too rapid decompression and in one case, they treated the symptoms by returning the patient to the high pressure air.

In 1855, Littleton (*71*) described 25 cases of illness in caisson workers employed over several months in the construction of a bridge across the Tamar at Saltash, Cornwall in England. In the course of this construction, caissons were driven to a depth of 85 ft. In the severe form of the illness, workers were seized a few minutes after decompression with pains in the limbs, paralysis, and unconsciousness. In less severe cases, there were simply pains in the limbs and joints. In attempting to explain these symptoms, Littleton recalled that Robert Boyle in the 17th century had observed a conspicuous bubble of air moving to and fro in the aqueous humor of the eye of a viper that had been decompressed and Littleton believed that the cause of the decompression symptoms might be the "extrication of air" occasioning pressure on the brain. As a method of preventing these symptoms, Littleton recommended gradual application and reduction of pressure.

In 1872, Friedberg (*66*) reviewed the historical development of compressed air work. In commenting on the development of the caisson by Triger, Friedberg noted that von Derschau in 1826 had used air compression for raising water and queried whether Triger got his idea from this. Friedberg reviewed the symptoms manifested by workers exposed to high pressure and to decompression and stated that there was a danger not only in decompression but also in remaining at pressure. He called attention to disturbances of the ear as a result of changing pressure and claimed that in breathing under pressure, the diaphragm descends lower because of compression of intestinal gases. Moderate compression such as used for therapeutic purposes results in a deeper, easier respiration but the higher pressures experienced in the caisson often resulted in cough and pains in the chest, according to Friedberg. It was also stated that there was acceleration of the metabolic processes, an increase in urinary excretion and a loss of weight. Workers claimed that they had greater muscular power while subjected to high pressure. Afterwards, workers felt unusually fatigued. It was believed that high pressure forced the blood from the surface to the interior of the body and that this accounted for the pallor of workers leaving the chamber. Subsequent experiences indicate that the peripheral circulation is apparently not disturbed as a result of high pressure. If decompression occurred too suddenly any of a number of symptoms might supervene. These included pains in the limbs, dyspnea and coughing, convulsions, paralysis (particularly of the legs and bladder), and stammering. Victims might fall unconscious and may die suddenly. According to Friedberg, these cases were reminiscent of the unconsciousness and sudden death sometimes seen by surgeons and obstetricians on entry of air into blood vessels in open wounds (air embolism). Friedberg believed that the rapid decompression of workers caused a sudden unloading of the excess of gas taken up during the rise of pressure. This rapid gas formation was thought to fill the blood with gas bubbles which interfered with the circulation of the blood in the heart and lungs and caused unconsciousness and death in the same way as severe acute air embolism. For the protection of workers in compressed air, Friedberg recommended exclusion of all but healthy individuals, limitation of hours of work to shifts of 4 hours each and not allowing a pressure of more than 3 atmospheres in excess of normal pressure. He advised a compression time of one-fourth hour and a decompression time at least as long; also, cooling and ventilation in the caisson, warm, dry clothes during the period of "locking out," and recompression for grave symptoms.

For a detailed study of bridge construction under compressed air, reference may be made to a paper published in 1874 by Malézieux (*72*). This reviews a large number of construction operations both in Europe and in the United States and contains a particularly good account of the medical problems which arose in connection with the building of the Brooklyn Bridge in New York between 1870 and 1873. Malézieux also referred to Denys Papin, born in 1674, who enunciated the idea of employing compressed air not only to maintain a flame alight under water but also to build underwater by means of a bell in which the air should be continually renewed.

No account of the development of compressed air work in caissons and tunnels would be complete without reference to the work of Paul Bert. Bert's (*16*) book published in 1878 should be consulted as should a new article by Ackerknecht (*61*) which appeared in 1944, on Paul Bert.

One of the most important works in the 19th century on bridge construction using compressed air caissons is the history of the St. Louis Bridge published in 1881 by Woodward (*82*). This long monograph contains excellent photographs of the bridge in various stages of its construction together with drawings of the piers, abutments, etc. At the beginning of the construction, the men worked for 2 hours and on emerging from the lock some suffered slight paralysis. The pressure within the caisson at this time was at a maximum of 40 lb. per sq. in. Patients recovered within 2 to 3 days.

In St. Louis, paralysis in the lower limbs was noticed to be more common at depths beyond 60 ft. There were also pains in the joints and in the stomach. So long as the paralytic symptoms were painless, they were not regarded as very serious. A workman walking about with a defective gait and slight stoop was at first looked upon as a fit object for the jokes of his fellow workers and a case of paralysis and cramps soon became popularly known by the name of "Grecian bend" after a certain type of posture affected in walking by certain women at the time. It is of interest that as a method of treating and preventing the "bends," it was suggested that workmen wear bimetalic amulets or "galvanic bands" which were supposed to generate electricity and so prevent and relieve the ill effects of decompression. Woodward's monograph is useful as a source of several post-mortem reports of workmen who died at the St. Louis bridge construction. In all, a total of about 600 men were engaged in the air chambers of the east and west piers and the eastern abutment. Out of this number, a total of 119 cases of decompression sickness were reported. Fourteen laborers died and 8 post-mortem examinations were carried out.

In 1884, Nowak (*73*) published a summary of the medical aspects of raised atmospheric pressures in caissons. This paper reviews the effects of high pressure and decompression on the health of the workmen in a number of construction operations in both the United States and in Europe.

In 1903, Batard-Razelière (*62*) described the caisson operations in connection with the building of a wet dock at the Port of Marseille in France. This project was carried out by Guèrard and Batard-Razelière as chief engineers. The foundations of the walls of the quay were built with floating caissons which could be moved from place to place as required. Batard-Razelière's article includes good illustrations of these caissons.

The medical problems faced in the construction of the Hudson River tunnels of the Hudson and Manhattan Railroad Company were described in 1910 by Jacobs (*69*). In 1895, the author was invited to report upon the practicability of completing the old Hudson River tunnel operations which had been suspended on many occasions and taken up again under new management. The work was commenced in February 1902 and the course of the construction is described by Jacobs. A medical staff was maintained and all workers given compulsory medical examinations; the carbon dioxide in the air was frequently analyzed and adequate ventilation was maintained. At pressures of 30 lb. per sq. in. or less, workers carried out one shift of 8 hours a day. At

pressures over 30 lb. per sq. in. they remained in the caisson for two shifts of 3 hours each, with an intermission of 3 hours for rest. The work went on continuously for 24 hours a day and 8,400 men were employed when the construction was progressing at its maximum rate. In all, 2,900 men were passed by the medical officer to work at pressures of over 20 lb. per sq. in. and 11,400 men were passed to work at pressures under 20 lb. per sq. in. There were 1,575 cases of compressed air illness requiring medical treatment and among these, 3 deaths occurred. Jacob's paper contains an additional account of the engineering problems associated with tunnel construction.

For an account of work under compressed air at the Boulac Bridge over the Nile, attention is invited to a paper by Knowles (*70*) 1911. At the point where the bridge was constructed, the Nile is 250 m. wide and 20 m. deep. Caissons were used in excavating for the piles. In this operation, 493 men were employed. There were 115 cases of illness involving 100 men and 4 fatalities occurred at pressures of 16, 33, 38, and 43 lb. per sq. in. The fatal cases are described. After these deaths, the hours of work were reduced and the period of decompression lengthened. Up to 40 lb. per sq. in., workers remained in the chamber for 8 hours during the day. At pressures between 40 and 45 lb. per sq. in., 6-hour shifts were allowed, whereas, between 45½ and 50 lb. per sq. in., workers were permitted to work for 4-hour periods only. At pressures up to 35½ lb. per sq. in., the decompression rate was fixed at 1.4 lb. per minute. Between 35½ and 42½ lb. per sq. in., the minimal total time of decompression was 35 minutes. Between 42½ and 45½ lb. per sq. in., the total decompression time was 40 minutes. At 45½ to 50 lb. per sq. in., the total time was fixed at 45 minutes. Inhalation of oxygen was considered to benefit cases of compressed air illness, particularly where a disturbance of the heart was supected. No recompression chamber was used.

For a fairly brief description of the problems of compressed air illness in bridge building in which early observations of the effect of raised atmospheric pressures on caisson and tunnel workers is given, the reader may consult a paper by Oliver published in 1933-34 (*74*). For further details of the history of bridge construction for tunneling operations using compressed air, the reader should turn to reports by Smith (*76*) 1873, Singstad (*39*) 1936, Keays (*1089*) 1912, and Levy (*2181*) 1922.

61. Ackerknecht, E. H. Paul Bert's triumph. *Bull. Hist. Med.*, (Suppl. No. 3. *Essays in the history of medicine presented to Professor Arturo Castiglioni on the occasion of his seventieth birthday April 10, 1944*), 1944, pp. 16–31. [R]

62. Batard-Razelière, [ ]. Travaux de construction du bassin de la pinède. *Ann. Ponts Chauss.*, (Mém. et Doc.) 1903, Sér. 8, *12* (4. trim.): 9–64. [P]

63. Blavier, [ ]. Rapport adressé à M. le sous-secrétaire d'État des travaux publics, en date du 17 février 1846, sur le procédé suivi à Douchy pour traverser des nappes d'eau considérables, au moyen de l'air comprimé. *Ann. Min., Paris*, 1846, Sér. 4, *9:* 349–364. [C]

64. Detmold, W. The physiological effects of highly-condensed air upon the human body. *N. Y. J. Med.*, 1843, *1:* 185–189.

65. Fleury, E. Lamé. La propriété souterraine en France. *Rev. deux Mondes*, 1857, Sér. 2, *12:* 182–219. [C]

66. Friedberg, H. Ueber die Rücksichten der öffentlichen Gesundheitspflege auf das Arbeiten in comprimirter Luft. *Dinglers J.*, 1872, *205:* 509–519. [B, R]

67. Henderson, Y. The contributions of J. S. Haldane to industrial hygiene. *J. industr. Hyg.*, 1936, *18:* 363–366.

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71. Littleton, T. Effects of submarine descent. *Ass. med. J.*, 1855, *3:* 127–128. [C]

72. Malézieux, [ ]. Fondations à l'air comprimé. *Ann. Ponts Chauss.*, (Mém. et Doc.) 1874, Sér. 5, 7 (1. trim.): 329–402. [C, P]

73. Nowak, J. Die hygienische Bedeutung des Luftdruckes. *Z. Ther. Einbzhung. Elect. Hydrother.*, 1884, *2:* 17–21. [R]

74. Oliver, T. Compressed air illness in colossal bridge building. *Arch. Gewerbepath. Gewerbehyg.*, 1933–34, *5:* 313–318. [R]

75. Pol, B. and T.-J.-J. Watelle. Mémoire sur les effets de la compression de l'air appliquée au creusement des puits à houille. *Ann. Hyg. publ., Paris*, 1854, Sér. 2, *1:* 241–279. [C, P]

76. Smith, Andrew H. *The effects of high atmospheric pressure, including the caisson disease.* Brooklyn, Eagle Print, 1873, 53 pp. [C, P]

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80. Triger, [ ]. Emploi de l'air comprimé pour les épuisements. Roches attaquées par la poudre dans des puits où l'air est comprimé à trois atmosphères. Application de l'air comprimé pour le sauvetage des bâtiments. *C. R. Acad. Sci., Paris*, 1845, *21:* 233–234. [C]

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Technical Procedures and Research Apparatus in Compressed Air, Diving, and Submarine Medicine

THE literature included under this title is admittedly not complete. The papers selected have been chosen principally because they have been referred to in reports dealing with submarine and compressed air medicine. For more complete descriptions of technical procedures, reference should be made to such standard works as Peters and Van Slyke (*119*) 1932.

I. GAS ANALYSIS IN AIR AND IN BLOOD

Reports by the following authors have been encountered in the literature dealing with oxygen and carbon dioxide concentrations in respiratory gases and blood in closed spaces such as submarines, caissons, and tunnels: Bert (*85*) 1873; Mosso and Marro (*117*) 1903; Waller and Collingwood (*143*) 1903-4; Brown (*86*, *87*, *88*) 1911, 1914, and 1915; Barcroft and Nagahashi (*84*) 1921; Van Slyke and Stadie (*141*) 1921; Hill (*104*) 1922; Carpenter (*92*) 1923; Knipping (*111*) 1924; Van Slyke and Neill (*136*) 1924; Nicloux and Roche (*118*) 1925; Ledig and Lyman (*113*) 1927; Van Slyke (*133*) 1927; Du Vigneaud (*95*) 1927-28; Carpenter, Fox, and Sereque (*93*) 1929; Lubin and Bullowa (*116*) 1929-30; Bullowa and Lubin (*90*) 1931; Van Slyke and Sendroy (*138*) 1932; Van Slyke, Sendroy, and Liu (*139*) 1932; Swift (*132*) 1932-33; Holsomback (*106*) 1938; Anthony (*83*) 1939; Dierkesmann (*94*) 1939-40; Loeschcke, Opitz, and Schoedel (*115*) 1939-40; Rein (*120*) 1939-40; Eckman and Barach (*97*) 1941; von Issekutz (*110*) 1941; Simonson (*131*) 1941; Sartori (*121*) 1942; Scholander (*125*, *126*, *127*) 1942; and Iliff, Kinsman, Hill, and Lewis (*108*) 1943. For a description of micro methods of gas analysis, reports by Campbell and Taylor (*91*) 1935 and Scholander (*123*, *124*, *125*) 1942 should be consulted. A method for the determination of gas content of tissue was published by Scholander (*126*) in 1942.

The literature on the analysis of carbon monoxide in blood and in air is large and many modern studies have been conducted as classified projects. The following list is therefore not complete but is given as a guide. The reader will find a detailed description of methods of carbon monoxide analysis and further references to methods of analysis in a monograph by Von Oettingen (*142*) published in 1944. In addition, reports by the following authors may be referred to: Gréhant (*100*) 1893, Haldane (*101*, *102*) 1895 and 1896, Levy and Pécoul (*114*) 1905, Krogh (*112*) 1918-19, Van Slyke and Salvesen (*137*) 1919, Hartridge (*103*) 1920-21, Schmidt (*122*) 1931, Sendroy (*130*) 1932, Frevert and Francis (*98*) 1934, Dyakov (*96*) 1936-37, Gigon and Noverraz (*99*) 1942, Horvath and Roughton (*107*) 1942, Scholander and Roughton (*128*) 1942, and Holden (*105*) 1943.

For a simple method of helium analysis, a report by Schwentker and Fallin (*129*) 1937 may be referred to and for a description of the analysis of hydrogen, two papers by Van Slyke and Hanke (*134*, *135*) 1932 should be consulted. Isoard (*109*) 1885 described the use

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98. Frevert, H. W. and E. H. Francis. Improved analyzer for carbon monoxide in air. *Industr. Engng. Chem.*, Analytical edition, 1934, *6:* 226–228. [P]

99. Gigon, A. and M. Noverraz. Une méthode simple et sensible de détermination de l'oxyde de carbone dans l'air atmosphérique. *Schweiz. méd. Wschr.*, 1942, *72:* 1356–1358. [P]

100. Gréhant, N. Application du grisoumètre à la recherche médico-légale de l'oxyde de carbone. *C. R. Acad. Sci., Paris*, 1893, Sér. 9, *5:* 162–164.

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102. Haldane, J. The detection and estimation of carbonic oxide in air. *J. Physiol.*, 1896, *20:* 521–522. [P]

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121.* Sartori, A. Descripción y manejo del aparato para análises de gases de Haldane-Henderson-Bailey. *Rev. méd., Cordoba*, 1942, *30:* 235–248.

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II. RESPIRATORY APPARATUS

More complete bibliographies of the literature dealing with respiratory apparatus are to be found in *A Bibliography of Aviation Medicine* (Hoff and Fulton (*3*) 1942) and the Supplement to that bibliography by Hoff, Hoff, and Fulton (*4*) 1944. A large body of information is also contained in the classified literature published during World War II. For further information, the reader may consult papers by the following authors: Mosso (*158*) 1904; Brat (*148*) 1906; Larsen (*157*) 1920; Fleisch (*156*) 1925; Sudeck and Schmidt (*162*) 1926; Dana (*151*) 1929; Deutsch (*153*) 1933; Ziegler (*163*) 1933; Anthony (*145*) 1935;

Fegler (*155*) 1938; Anthony and Rohland (*146*) 1939; Beyne and Gougerot (*147*) 1939; Enghoff (*154*) 1939; Cournand, Darling, Mansfield, and Richards (*150*) 1940; Darling, Cournand, and Richards (152) 1940; Cournand, Baldwin, Darling, and Richards (*149*) 1941; Adriani (*144*) 1941; Scholander and Edwards (*161*) 1942; Pitton, Schlack, and Restarski (*160*) 1943; and Nickerson, King, and Curtis (*159*) 1944.

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156. Fleisch, A. Der Pneumotachograph; ein Apparat zur Geschwindigkeitsregistrierung der Atemluft *Pflüg. Arch. ges. Physiol.*, 1925, *209:* 713–722. [P]

157. Larsen, C. N. A new type of rebreather and other respiratory apparatus. *Air. Serv. Inform. Circ.*, 1920, *1*(99): 8–15. Also: 1923, *5*(403): 1–8. [P]

158. Mosso, A. La ventilation rapide des poumons au moyen d'un appareil qui fonctionne avec de l'air comprimé et de l'air raréfié. *Arch. ital. Biol.*, 1904, *41:* 192–200. Also in Italian: *R. C. Accad. Lincei*, 1904. Ser. 5, *13* (1): 167–174.

159. Nickerson, J. L., B. G. King, and H. J. Curtis. A small recording spirometer. *Rev. sci. Instrum.*, 1944, *15:* 12–13. [P]

160. Pitton, R. D., C. A. Schlack, and J. S. Restarski. Double-grooved mouthpiece for oral respiration in low and high barometric breathing. A preliminary report. *Nav. med. Bull., Wash.*, 1943, *41:* 1420–1424. [P]

161. Scholander, P. F. and G. A. Edwards. Volumetric microrespirometer for aquatic organisms. *Rev. sci. Instrum.*, 1942, *13:* 292–295. [P]

162. Sudeck, [ ]. and H. Schmidt. Ein neues Modell eines möglichst druckkonstanten Überdruckapparates. *Dtsch. Z. Chir.*, 1926, *197:* 1–9. [P]

163. Ziegler, E. E. A new measurement of oxygen absorbing power. *J. Aviat. Med.*, 1933, *4:* 119–129. [P]

III. APPARATUS FOR TESTING VISUAL FUNCTIONS

For references on techniques and apparatus for the testing of visual functions, the literature quoted by Hoff and Fulton (*3*) 1942; Hoff, Hoff, and Fulton (*4*) 1944; and Fulton, Hoff, and Perkins (*2*) 1945 should be consulted. Most of this literature is not exclusively concerned with problems related to submarine or diving activities or subaqueous construction work. However, much work on visual function has been carried out under the auspices of medical research laboratories attached to the submarine service. Most of this latter work is to be found in classified reports prepared during World War II. This literature should be consulted by those having access to it. Further information on testing of visual functions may be found in reports by the following authors: Ferree and Rand (*164*, *165*) 1920 and 1936, Howard (*170*) 1923, Herbolsheimer (*169*) 1930, Greene (*167*) 1937, Litinskiy (*171*) 1937, Weaver (*173*) 1938, White (*174*) 1938, Haig and Lewis (*168*) 1939, Fisk and Stoddard (*166*) 1940, and Simpson and Freeman (*172*) 1940.

164. Ferree, C. E. and G. Rand. Lantern and apparatus for testing the light sense and for determining acuity at low illuminations. *Amer. J. Ophthal.*,1920 Ser. 3, *3:* 335–340. [P]

165. Ferree, C. E. and G. Rand. An instrument for measuring dynamic speed of vision, speed of accommodation and ocular fatigue. *Arch. Ophthal., Chicago*, 1936, Ser. 2, *15:* 1072–1087. [P]

166. Fisk, C. and S. E. Stoddard. A device for measuring differential sensitivity to light. *Amer. J. Psychol.*, 1940, *53:* 291–292. [P]

167. Greene, R. N. Attachment for depth perception apparatus. *J. Aviat. Med.*, 1937, *8:* 100. [P]

168. Haig, C. and J. M. Lewis. Simple method of measuring brightness threshold of dark adapted eye at all ages. *Proc. Soc. exp. Biol., N. Y.*, 1939, *41:* 415–418. [P]

169. Herbolsheimer, A. J. A new instrument for testing for diplopia. *J. Aviat. Med.*, 1930, *1:* 102. [P]

170. Howard, H. J. A new apparatus for testing accommodation. *Air Serv. Inform. Circ.*, 1920, *1*(99): 86–89. Also: 1923, *5*(403): 71–74. [P]

171.* Litinskiy, G. A. [Apparatus for testing stereoscopic vision.] *Vyestn. Oftalm.*, 1937, *10:* 116–120.

172. Simpson, R. M. and G. L. Freeman. An instrument for determining visual thresholds. *Amer. J. Psychol.*, 1940, *53:* 289–290. [P]

173. Weaver, W. R. An aid in the dark room. *Flight Surg. Top.*, 1938, *2*(4): 227

174. White, S. An aid in the measurement of depth perception. *Flight Surg. Top.*, 1938, *2*(3): 161, 1 pl.

IV. CHAMBERS

In 1891, Legay (*177*) described the construction and functioning of compressed air chambers. Similar descriptions were given by Thomson, Yaglou, and Van Woert (*179*) 1932 and Jongbloed and Noyons (*176*) 1933. Metabolism chambers were described by Benedict and Homans (*175*) 1911 and Pierce (*178*) 1935-36. Further references to compression chambers are found on page 308 in the section on therapeutic effects of gases under raised atmospheric pressures and in literature quoted by Hoff and Fulton (*3*) 1942; and Hoff, Hoff, and Fulton (*4*) 1944. For numerous details on the construction of compression and decompression chambers, the unpublished classified literature must be consulted or information requested from commercial companies manufacturing such equipment.

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175. Benedict, F. G. and J. Homans. A respiration apparatus for the determination of the carbon dioxide produced by small animals. *Amer. J. Physiol.*, 1911, *28:* 29–48.

176. Jongbloed, J. and A. K. Noyons. Demonstration eines pneumatischen Kabinetts für Unter-, und Überdruck. *Acta brev neerl. Physiol.*, 1933, *3:* 158.

177. Legay, [ ]. Des progrès réalisés dans la construction et le fonctionnement des chambres à air comprimé. *Bull. gén. Thér., Paris*, 1891, *120:* 163–168.

178. Pierce, H. F. A metabolism chamber which automatically maintains a constant partial pressure of oxygen. *J. Lab. clin. Med.*, 1935–36, *21:* 317–322.

179. Thomson, R. M., C. P. Yaglou, and A. B. Van Woert. A pressure chamber installation for studying the physiologic effects of pressures varying from 6 to 60 pounds per square inch absolute. *J. industr. Hyg.*, 1932, *14:* 57–68.

V. AIR COMPRESSORS

Descriptions of air compressors for medical use were given by Kuhn (*181*, *182*) 1909 and Beams, Casteel, and King (*180*) 1937 have also published descriptions of air compressors. The subject of compression pumps does not come strictly within the province of this Sourcebook although it is of considerable medical importance that compressors be so constructed as to deliver only pure air and that provision be made against sudden accidental failure of pressure.

180. Beams, H. W., A. T. Casteel and R. L. King. An economical air compressor. *Science*, 1937, *86:* 428.

181. Kuhn, F. Der Luftkompressor im Krankenhause. *Dtsch. med. Wschr.*, 1909, *35:* 1966–1968.

182. Kuhn, F. Der Luftkompressor im Krankenhause. II. Lungenüberdruck mittels Luftkompressors und Maske. *Dtsch. med. Wschr.*, 1909, *35:* 2215–2217.

VI. OTHER TECHNICAL PROCEDURES AND APPARATUS

Further papers on technical procedures and apparatus which have been encountered in the course of the compilation of this Sourcebook are those published by the following authors: Recknagel (*191*) 1893, Cogliati (*184*) 1905, Ellis and Larsen (*185*) 1920, Miles (*188*) 1920, Marage (*186*) 1921, Vernon (*192*) 1927, Broda (*183*) 1937, Marczewski and Rosnowski (*187*) 1938, Pol (*190*) 1938, and Mizzi (*189*) 1939.

183. Broda, B. O technice pomiarów pH w koloidach elektrodą wodorową S. Marczewskiego. (La technique des mesures du pH dans les colloides prises à l'aide d'électrode d'hydrogène de Marczewski.) *Polsk. Przegl. Med. Lotn.*, 1937, *6:* 110–122. (With German summary.)

184. Cogliati, A. Generador automático de oxígeno continuo con recargador para continuar su producción y lavador. *Sem. méd., B. Aires*, 1905, *12:* 1014–1017.

185. Ellis, M. M. and C. N. Larsen. A device adapting the Barany chair to rebreather tests. *Air Serv. Inform. Circ.*, 1920, *1*(3): 36–38.

186. Marage, [ ]. Le repérage des sous-marins et le seuil de l'audition. *Bull. Acad. Méd. Paris.*, 1921, Sér. 3, *85:* 99–102.

187. Marczewski, S. and M. Rosnowski. Wydolność moderacyjna krwi, a zjawisko elektrowłoskowatości. (Pouvoir tampon du sang et phénomène électrocapillaire.) *Polsk. Przegl. Med. Lotn.*, 1938, *7:* 16–42. (With French and English summaries.)

188. Miles, W. R. A pursuit pendulum. *Psychol. Rev.*, 1920, *27:* 361–376. [C]

189. Mizzi, A. Cronografo automatico M-G; un nuovo apparecchio registratore dei tempi di reazione. *Rass. Med. Lav. industr.*, 1939, *10:* 36–47.

190. Pol, W. Przyrząd sygnalizacyjny do badania daltonistów. (Appareil de signalisation destiné aux épreuves de daltoniens.) *Polsk. Przegl. Med. Lotn.*, 1938, *7:* 281–286. (Polish and French texts.)

191. Recknagel, G. Ueber Einrichtung und Gebrauch des Differenzialmanometers. *Arch. Hyg., Berl.*, 1893, *17:* 234–254.

192. Vernon, H. M. The wet Kata-thermometer as an index of the suitability of atmospheric conditions for heavy work. *J. industr. Hyg.*, 1927, *9:* 287–296

Special Anatomy, Physiology, and Biochemistry of Compressed Air, Diving, and Submarine Medicine

I. PHYSIOLOGICAL EFFECTS OF RAISED ATMOSPHERIC PRESSURES

A. GENERAL STUDIES

Very early in the use of caissons in mining, tunneling, and construction operations, it was discovered that subjecting the body to raised atmospheric pressure produced certain physiological and pathological responses. Notable among these were mechanical effects upon the ear, changes in the voice, and a certain sense of well-being and increased muscular power. Although some workers were unable to support the conditions of raised atmospheric pressure and other environmental factors present in the working chamber of the caisson, nevertheless, it was in general not the "locking in" or the actual stay under pressure that caused trouble, but rather the decompression or "locking out." Many studies have been carried out in caissons and tunnels on the effects of compression, and it is now clear that exposure to such environment does cause certain physiological changes. However, in investigating these studies, it must be borne in mind that the environment of the caisson not only imposes raised atmospheric pressure upon the organism but may also involve such factors as high humidity, extremes of temperature, poor ventilation, noxious gases, and heavy labor in mud and cold water. Therefore, the physiological adjustments which have been investigated are, strictly speaking, not to be attributed to compressed air alone.

In suggesting that compression of the atmosphere within the limits encountered in caisson and tunneling operations is relatively innocuous, it is not implied that the animal body is capable of adapting itself to any condition of air pressure. In deep sea diving, pressures are reached at which oxygen intoxication becomes a severe and limiting factor. References to the literature on this subject are found on page 163. Also, at great depths, there is a slowing of mental function and sluggishness of motor response attributed to the narcotic action of nitrogen under pressure, and the reader will find a description of this subject on page 162. In both oxygen intoxication and nitrogen narcosis, however, the effects upon the body are not to be ascribed to the influence of pressure *per se;* for example, if nitrogen is replaced by helium, the diver is capable of descent to much greater depths without adverse symptoms. As will be seen by consulting the section on the biology of very high hydrostatic pressure on page 85, living organisms including bacteria, protozoa, invertebrate and vertebrate marine animals as well as the isolated tissues of higher animals are capable of withstanding pressures far in excess of any encountered in industrial or military operations without functional depressions. Hydrostatic pressures are reached, however, at which physiological processes are brought to a standstill. At these extremely high hydrostatic pressures, living protoplasm is actually compressed and tends to become coagulated. Within the pressure ranges, at present encountered or likely to be encountered in diving or other subaqueous oper-

ations, living tissues support the increased pressure without harm.

Guérard (*203*) 1854 called attention to pain in the ears on going under pressure and also reported a slowing of the pulse rate of approximately 10 to 20 beats per minute. He also referred to observers who detected no change in pulse rate in early caisson workers. The respiration was stated to become slower and more shallow and many early investigators reported that breathing was easier in compressed air. This latter observation was in part the basis for the wide use of compressed air chambers in the 19th century as a therapeutic procedure in the management of asthma, chronic bronchitis, and other acute and chronic respiratory diseases. Many physiological observations on the physiological action of raised atmospheric pressure were made in the course of such treatments. These findings are reviewed in the section on the therapeutic effects of gases under raised atmospheric pressures. As the reader will discover on consulting that literature, the pressures used in the therapeutic compression chambers were nearly all less than 2 atmospheres (absolute) and in most instances were not greater than one-half atmosphere above normal pressure.

An early study on the physiological effects of compressed air on hearing, vision, olfaction, taste, and cutaneous sensation, as well as muscular contraction, circulation, and respiration, was carried out by Foleÿ (*202*) in 1863. von Liebig (*212*) 1871 also reviewed the physiological action of raised atmospheric pressures. He found that the respiratory rate was slowed and the volume of respiration decreased as the pressure increased. There was a reduction of carbon dioxide output at high pressures. The pulse rate was reduced. von Liebig also drew attention to a sense of increased energy in caisson workers and divers when under pressure.

Paul Bert (*197*) 1874 minimized the physiological effects of changes in barometric pressures with the exception of very rapid changes in their influence on the ear and oxygen poisoning at higher pressure levels. The reader is referred to three papers by Paul Bert (*195*, *196*, *198*) published in 1870, 1871-74, and 1874 as well as his large monograph (*16*) 1878. Bert's work up to 1874 was reviewed by Lereboullet (*210*) 1874.

Hirt (*205*) in 1874 published a long report which contained a description of the action of compressed air on the depth and rate of respiration, blood pressure, peripheral circulation, hearing, taste, and cutaneous sensation.

For further allusion to early work on the effect of air pressure on human life, the reader is referred to a two-volume work published in 1875 by Jourdanet (*207*). This study is largely concerned with the effects of high altitudes but is of some interest since the author advanced the fantastic notion that the atmospheric pressure in the past used to be greater than at present times and that high air pressure on coastal plains forced man into mountains and high plateaus.

In a brief statement published in 1896 (*220*), the effects of entering the caisson were listed as follows: (a) tingling in the ears, (b) pain in the ear drums, (c) temporary vertigo, (d) dilatation of the heart, (e) raised arterial blood pressure, and (f) slowing of respiration. All symptoms were reported to be temporary. Prolonged work in the caisson was stated to cause paleness of the skin with varicosity of the capillaries of the nose and cheeks, hypertrophy of the heart, bradycardia, and leucocytosis. All symptoms were believed to be referable to raised tensions of carbon dioxide in the bad air of caissons. The characteristic pallor of caisson workers has been repeatedly ascribed to the effect of raised atmospheric pressure in reducing peripheral circulation. As will be seen, however, there is evidence that peripheral circulation is not significantly affected.

Lewis (*211*) in 1898 stated that exposure to raised atmospheric pressure causes a slowing of respiration, a deceleration of the pulse and an increased secretion of saliva and urine.

Kabrhel (*208*) 1903 stated that when the pressure reached a level of 2.5 atmospheres (absolute), the voice becomes metallic and nasal. The pulse rate was stated to be reduced and respiration was also slowed. A slight increase in body temperature was believed to

occur. The author also reported an increase in the concentration of oxygen and gaseous nitrogen in the blood. The report continued with a description of the effects of rapid decompression and a discussion of the experiments of various authors on air embolism. The value and procedure of therapeutic recompression were also discussed.

Hill and Greenwood (*204*) 1905–6 subjected themselves to raised atmospheric pressures up to 92 lb. in a chamber for short periods of time. They drew attention to pains in the ears during compression. The sensation of pressure ceased when the pump stopped and the pressure in the chamber was maintained constant. Voice alterations were noticeable at 2 atmospheres (absolute) and very marked at 4 atmospheres (absolute). Speech had a nasal, metallic quality and at 4 atmospheres (absolute) subjects were unable to whistle or whisper. There was a sense of anesthesia over the tongue and lips. One author experienced a slight slowing of the pulse while the other showed no change in heart rate even at 6 atmospheres (absolute). No change was found in the quantity of carbon dioxide exhaled.

Stettner (*218*) 1910 reported on alterations in vision, speech, hearing, respiratory rate, blood flow, heart rate, blood pressure, body temperature, metabolism, urinary nitrogen, and blood gases.

Murakami (*216*) 1931, reported a rise in pulse rate in divers during descent. In some cases, however, there was no alteration in the heart rate. The blood pressure was stated to rise and there were pains in the ears. The urinary reaction was alkaline and some albuminuria was also reported. The carbon dioxide content of the helmet was found to be 2 to 3 percent. It appears, therefore, that the symptoms were those of carbon dioxide intoxication as much as physiological effects of raised pressure. One diver was stated to have descended to a depth of 54.9 m. without symptoms.

Hosokawa (*206*) 1936 reported experiments in which human subjects were taken to pressures of 30 to 50 lb. and studies carried out on the blood and respiration. A decrease in blood lactic acid was reported and the blood pH was stated to shift toward the acid side. The oxygen saturation in the blood was diminished and there was a hydremia.

Behnke (*194*) 1939 discussed the effects of raised barometric pressure on the ear. This paper also reviews Behnke's previous work in submarine physiology.

According to Marquort and Rietz (*214*) 1939, there is no basis for the supposed alteration in respiratory gas exchange at pressures up to 3.75 atmospheres (absolute). However, breathing was said to be deeper and slower at such pressure. No change was found in vital capacity. The frequency of the pulse was said to drop and there was a tendency toward a fall in blood pressure. The electrocardiogram was stated to indicate a change in position of the heart due to deeper descent of the diaphragm. There was, however, no alteration in conduction of the impulse or its potential. No changes were found in the electrocardiograms of workers who had been exposed to the environment of the caisson for many years. There was a tendency toward a reduction in the red blood cell count during exposure to high pressures with a return to normal on decompression. However, no evidence of anemia after rapid daily exposures to high pressure could be found. The blood chlorides were within normal limits and a rise in blood protein values was reported. The sedimentation rate remained normal.

For further general studies on the physiological effects of compression, the reader is referred to articles by Michaelis (*215*) 1872, Sukhorsky (*219*) 1885, Lecercle (*209*) 1907, Rubner (*217*) 1907, Damant (*199*) 1930, Maciel (*213*) 1937, and Baetjer (*193*) 1943.

193. Baetjer, A. M. The effects of abnormal atmospheric pressures. Pp. 91–100 in: *The principles and practice of industrial medicine.* Edited by Fred J. Wampler. Baltimore, The Williams & Wilkins Company, 1943, xiv, 579 pp.

194. Behnke, A. R. Medical problems relating to diving, underwater construction, and submarines. *Pacif. Sci. Congr.*, 1939, *6:* 85–89. [M, R]

195. Bert, Paul. *Leçons sur la physiologie comparée de la respiration.* Paris, J.-B. Baillière et Fils, 1870, xxxii, 588 pp. [C, R]

196. Bert, P. Recherches expérimentales sur l'influence que les changements dans la pression barométrique exercent sur les phénomènes de la vie. *C. R. Acad. Sci., Paris*, 1871, *73:* 213–216; 503–507. 1872, *74:* 617–621. 1872, *75:* 29–33, 88–92; 491–494; 543–547. 1873, *76:* 443–446; 578–582; 1276–1280; 1493–1497. 1873, *77:* 531–535. 1874, *78:* 911–914. [C, R]

197. Bert, P. Recherches expérimentales sur l'influence que les changements dans la pression barométrique exercent sur les phénomènes de la vie. *C. R. Acad. Sci., Paris*, 1874, *78:* 911–914. [C, R]

198. Bert, P. Recherches expérimentales sur l'influence que les modifications dans la pression barométrique exercent sur les phénomènes de la vie. Abstr: *Nature, Paris*, 1874, *2*(1): 306–308; 355–358; 402–406. [C, R]

199. Damant, G. C. C. Physiological effects of work in compressed air. *Nature, Lond.*, 1930, *126:* 606–608. [R]

200. DuBois, E. F. Physiology of respiration in relationship to the problems of naval medicine. Part I. *Nav. med. Bull., Wash.*, 1928, *26:* 1–16; 247–256. [R]

201. DuBois, E. F. Physiology of respiration in relationship to the problems of naval medicine, Part II. Respiration in disease. *Nav. med. Bull., Wash.*, 1928, *26:* 256–270. [R]

202. Foleÿ, Antoine-Édouard. *Du travail dans l'air comprimé. Étude médicale, hygiénique et biologique faite au pont d'Argenteuil.* Paris, J.-B. Baillière et Fils, 1863, 136 pp. [B, R]

203. Guérard, A. Note sur les effets physiologiques et pathologiques de l'air comprimé. *Ann. Hyg. publ., Paris*, 1854, Sér. 2, *1:* 279–304. [R]

204. Hill, L. and M. Greenwood. The influence of increased barometric pressure on man. *Proc. roy. Soc.*, 1905–06, B, *77:* 442–453. [R]

205. Hirt, L. Gewerbe-Krankheiten. Die in Folge der Einathmung verschiedener Gase, Daempfe und Duenste auftretenden gewerblichen Erkrankungen ("Gas-Inhalationskrankheiten"). Nebst einem Anhang über den Einfluss der comprimirten Luft auf die Gesundheit der Arbeiter. *Handb. spec. Path. Ther.*, 1874, *1:* 381–468.

206. Hosokawa, S. Die Beiträge zur pathologischen Physiologie in der druckveränderten Atmosphäre. *Bull. nav. med. Ass. Japan*, 1936, *25*(2): (Japanese text pagination), 71–72; (English text pagination), 7–9. (In Japanese with German summary.)

207. Jourdanet, D. *Influence de la pression de l'air sur la vie de l'homme. Climats d'altitude et climats de montagne.* Paris, G. Masson, 1875, 2 vols. Abstr: *Nature, Paris*, 1875, *3*(1): 341–350; *Nature, Lond.*, 1875, *12:* 472–474. [C]

208. Kabrhel, G. Hygiene der Luftkompression. Nach neueren Arbeiten dargestellt. *Hyg. Rdsch.*, 1903, *13:* 161–188. [R]

209. Lecercle, [ ]. La pression atmosphérique. *Clinique, Paris*, 1907, *2:* 410–412.

210. Lereboullet, L. De l'influence que les modifications dans la pression barométrique exercent sur les phénomènes de la vie. *Gaz. hebd. Méd. Chir.*, 1874, Sér. 2, *11:* 491–493; 507–511. [R]

211. Lewis, F. T. The physiological effects of compressed air. *Boston med. surg. J.*, 1898, *139:* 338–341.

212. Liebig, G. von. Ueber den Einfluss der Veränderungen des Luftdruckes auf den menschlichen Körper. *Dtsch. Arch. klin. Med.*, 1871, *8:* 445–466. [R]

213. Maciel, H. Effeitos das variações da pressão atmospherica sobre o organismo humano; tubistas, escaphandristas, alpinistas e aviadores. *Brasil-med.*, 1937, *51:* 77–86.

214. Marquort, W. and J. Rietz. Physiologische Untersuchungen und Beobachtungen an Druckluftarbeitern. *Z. ges. exp. Med.*, 1939, *106:* 684–703. [M, R]

215. Michaelis, [ ]. Ueber die Wirkung des erhöhten und verminderten Luftdruckes auf den menschlichen Körper. *S. B. Isis Dresden*, 1872, pp. 37–42.

216. Murakami, S. The effect on the human body of the diving operation and also of the ascent process. *Bull. nav. med. Ass. Japan*, 1931, *20*(3): (Japanese text pagination), 1–16; (English text pagination), 1–2. (In Japanese with English summary.)

217. Rubner, Max. *Lehrbuch der Hygiene. Systematische Darstellung der Hygiene und ihrer wichtigsten Untersuchungs-methoden.* Leipzig, Wien, Franz Deuticke, 1907, 1029 pp.

218. Stettner, E. Über Caissonkrankheit mit pathologischanatomischer Beschreibung eines Falles. *Würzburg. Abh. prakt. Med.*, 1910, *11:* 285–317. [R]

219. Sukhorsky, N. [Effect of compressed air on the respiratory function in healthy and sick subjects.] *Vo.-med. Zh., Spb.*, 1885, *152*(3): 65–202.

220. Anon. Maladie professionnelle due au travail dans les caissons pneumatiques. *Ann. Hyg. publ., Paris*, 1896, Sér. 3, *36:* 180–181.

B. VOICE; WHISTLING

Heller, Mager, and von Schrötter (*221*) 1897 discussed von Liebig's explanation of the inability of whistling at raised atmospheric pressures. von Liebig held that the expired air was slowed and that there was a prolongation of the expiratory act. A certain velocity of air was necessary to bring forth a tone. The authors felt that von Liebig's explanation was inadequate. They considered that the action of the changed density of the medium on the sounding column of air is the cause of inability to make a sound, since the sound-producing mechanism is adjusted to certain pressure limits.

221. Heller, R., W. Mager, and H. von Schrötter. Bemerkung zu dem Aufsatze des Herrn Hofrath Dr. G. v. Liebig: "Warum man unter einem stark erhöhten Luftdrucke sowohl, wie unter einem start verminderten nicht mehr pfeifen kann." *Münch. med. Wschr.*, 1897, *44:* 362–363.

C. TASTE OF OXYGEN AND NITROGEN AT HIGH PRESSURES

At normal barometric pressure, oxygen and nitrogen are tasteless. According to Case and Haldane (*222*) 1941 if air is breathed at 6 to 7 atmospheres (absolute), there is a sweetish, acid taste due to oxygen; at 10 atmospheres of air, a metallic taste is noticed which was stated to be due to nitrogen under pressure. This taste is not detected if the nitrogen is replaced by oxygen or by helium.

222. Case, E. M. and J. B. S. Haldane. Tastes of oxygen and nitrogen at high pressures. *Nature, Lond.*, 1941, *148:* 84. [P]

D. EAR, NOSE, AND THROAT

For a further analysis of the effects of pressure upon the ear, nose, and throat, the reader should consult the literature cited in the section on ear, nose, and throat disturbances. Reference should also be made to a paper by Heller, Mager, and von Schrötter (*228*) 1897 reporting observations on physiological changes of the voice and hearing as a result of changes in atmospheric pressure.

A report by Lester and Gomez (*232*) 1889–90 may be consulted. The studies reported by these authors were carried out on personnel working on the foundations of a bridge over the East River in New York. Subjects reported a feeling of pressure and fullness in the ears on "locking in" and cupping of the ear drums was visible on examination. Both bone and air conduction were diminished under increased pressure, bone conduction being more seriously affected. Loss of sensitivity to the high tones was said to be greater than for the lower tones. Loss of auditory acuity was directly proportional to increase in pressure. In some individuals, diminished hearing persisted for 24 to 48 hours, and all symptoms were intensified by colds or any involvement of the middle ear.

According to Charonsek (*224*) 1926–27, all symptoms in the middle or inner ear are referable to the air space in the middle ear, the lymph system of the middle ear or the blood and lymph system leading into the endocranium. Pressure changes could affect any one or more of these.

Behnke (*223*) 1940 reported that if equalization of pressure in the middle ear and sinuses is interfered with, pressure differentials of as little as 1 to 2 lb. can result in painful symptoms. Unequalized pressure may result in hemorrhage, congestion of the tissue, or separation of the epithelium and tunica propria from the wall. The tympanic membrane may be ruptured by a pressure differential of 5 to 10 lb. Tubal blockage was found to occur in 10 to 15 percent of 2,000 submarine personnel tested. The use of the pressure chamber to test for congestion and blockage was recommended. Nineteen deep-sea divers who had been diving for 5 to 15 years were found to have loss in auditory acuity for sounds at a frequency of 4,096. Behnke's paper should also be consulted for a discussion of the effects of pressure on gas equilibrium in the body, on nitrogen narcosis, oxygen intoxication, and bubble formation in decompression.

For a study of the effect of drum tension and middle ear pressures on hearing, the reader may refer to a paper by Fowler (*226*) 1920. Pohlman and Kranz (*236*) 1923 found that positive pressure in the external auditory canal decreased hearing in all cases, whereas negative pressures up to 10 cm. of water increased the auditory acuity. Above this level, hearing decreased again. The effects of intralabyrinthine pressure upon hearing have been discussed by Lorenz (*235*) 1932, Hughson (*229*) 1932 and Hughson and Crowe (*230*) 1932–33.

For a consideration of the effects of changes in middle ear pressure on auditory acuity, reference may be made to papers by Thompson, Howe, and Hughson (*238*) 1934–35; Loch (*233*, *234*) 1942; and Wever, Bray, and Lawrence (*240*) 1942. These latter investigators found in experiments on cats that an increase in pressure in the middle ear caused a decrease in the cochlear response and that this

decrease was more marked for the lower frequencies. The cochlear response was found to be susceptible to respiratory change, dropping sharply if ventilation was reduced. As the pressure in the middle ear was increased, a greater intensity of tone was required to give the same response for any given frequency. The pressure necessary to break the ear drum was found to vary with individual animals. It was observed that pressure in the middle ear caused a sharp drop in bone conduction followed by a rise and subsequent leveling off. Air conduction showed a gradual and continued fall. The investigators concluded that middle ear pressure exerts its principal action upon the ear drum, although minor effects evidently arise also in its action upon parts of the inner ear.

Other reports of interest in relation to pressure within the ear which may be consulted are those by Szász (*237*) 1926, Wagner (*239*) 1929–30, Yoshida (*241*) 1932, and Keibs (*231*) 1936.

223. Behnke, A. R. High atmospheric pressures; physiological effects of increased and decreased pressure; application of these findings to clinical medicine. *Ann. intern. Med.*, 1940, *13:* 2217–2228. [P, M]

224. Charonsek, G. Zur Mechanik des Drucksymptoms. *Z. Hals- Nas.- u. Ohrenheilk.*, 1926–27, *9:* 271–272.

225. Crowe, S. J. and W. Hughson. Eine neue Methode zur Untersuchung der Physiologie und Pathologie des Ohres. *Z. Hals- Nas.- u. Ohrenheilk.*, 1931–32, *30:* 65–76.

226. Fowler, E. P. Drum tension and middle ear air pressures; their determination, significance and effect upon the hearing. *Ann. Otol., etc., St Louis*, 1920, *29:* 688–694.

227. Hartridge, H. The ear as morphologically an apparatus for perceiving depth below sea-level. *J. Physiol.*, 1920–21, *54:* 244–247.

228. Heller, R., W. Mager, and H. von Schrötter. Beobachtungen über physiologische Veränderungen der Stimme und des Gehörs bei Änderung des Luftdruckes. Aus den Untersuchungen über "Luftdruckerkrankungen." *S. B. Akad. Wiss. Wien*, III Abt., 1897, *106*(1): 5–37. [P]

229. Hughson, W. A note on the relationship of cerebrospinal and intralabyrinthine pressures. *Amer. J. Physiol.*, 1932, *101:* 396–407.

230. Hughson, W. and S. J. Crowe. Experimental investigation of the physiology of the ear. *Acta oto-laryng., Stockh.*, 1932–33, *18:* 291–339.

231. Keibs, L. Methode zur Messung von Schwellendrucken und Trommelfellimpedanzen in fortschreitenden Wellen. *Ann. Phys., Lpz.*, 1936, 5. Folge, *26:* 585–608.

232. Lester, J. C. and V. Gomez. Ueber die Einwirkung comprimirter Luft auf das menschliche Ohr, auf Grund der Beobachtungen, welche in dem Senkkasten der Brücke über den New East-River gemacht wurden. *Z. Ohrenheilk.*, 1889–90, *34:* 240–244. [P, R]

233. Loch, W. E. The effect on hearing of experimental occlusion of the eustachian tube in man. *Ann. Otol., etc., St Louis*, 1942, *51:* 396–405.

234. Loch, W. E. Effect of experimentally altered air pressure in the middle ear on hearing acuity in man. *Ann. Otol., etc., St Louis*, 1942: *51:* 995–1006.

235. Lorenz, H. Gehör und Labyrintdruck. *Acta oto-laryng., Stockh.*, 1932, *17:* 89–96.

236. Pohlman, A. G. and F. W. Kranz. The effect of pressure changes in the external auditory canal on acuity of hearing. *Ann. Otol., etc., St Louis*, 1923, *32:* 545–553.

237. Szász, T. Experimentelle Untersuchungen über den Innenohrdruck. *Z. Hals- Nas.- u. Ohrenheilk.*, 1926, *14:* 237–255.

238. Thompson, E., H. A. Howe, and W. Hughson. Middle ear pressure and auditory acuity. *Amer. J. Physiol.*, 1934–35, *110:* 312–319.

239. Wagner, R. Untersuchung der Luftdruckschwankungen im verschlossenen äusseren Gehörgang. II. Mitteilung. Ueber die pulsatorischen Schwankungen. *Z. Biol.*, 1929–30, *89:* 186–194.

240. Wever, E. G., C. W. Bray, and M. Lawrence. The effects of pressure in the middle ear. *J. exp. Psychol.*, 1942, *30:* 40–52.

241.* Yoshida, M. [Experimentelle Untersuchungen über die Veränderungen des Luftdrucks im äusseren Gehörgang, besonders über solche des Gehörorgans durch Pneumomassage des Trommelfells.] *Mitt. med. Akad. Kioto*, 1932, *6:* 2539–2541.

E. EFFECT OF RAISED ATMOSPHERIC PRESSURE ON THE PUPILS

Iwasaki (*242*) 1936–38 subjected rabbits to raised pressures of 5 to 60 lb. There was dilatation of the pupils which was reported to be directly proportional to the length of time under pressure and the extent of pressure. It did not, however, depend upon the speed of application of pressure. Atropine masked the reaction of the pupil to pressure.

242. Iwasaki, K. Experimentelle Untersuchungen über den Einfluss des höheren Luftdruckes auf das Kaninchenauge. I. Mitteilung. Über die Pupillenweite und Reizschwelle der Pupillenreaktion des Kaninchens

durch Halssympathikus-Reizung unter höheren Luftdruck. *Jap. J. med. Sci.*, III. Biophysics, 1936–38, *4:* 87–88 Proc. [P]

F. INTRACRANIAL VOLUME

Walsh (*243*) 1941 studied the action of reduced and raised atmospheric pressures on a 35-year-old woman with a right temporal craniotomy. At a barometric pressure of 247 mm. Hg (a simulated altitude of approximately 28,000 ft.), the scalp was raised 1 cm. by the increase in intracranial volume. Increasing the atmospheric pressure to ½ atmosphere above normal pressure resulted in a decrease in intracranial volume, as evidenced by a lowering of the scalp of 0.5 cm.

243. Walsh, M. N. Changes in intracranial volume on ascent to high altitudes and descent as in diving. *Proc. Mayo Clin.*, 1941, *16:* 220–221. Abstr: *J. Aviat. Med.*, 1941, *12:* 263.

G. MUSCULAR ACTIVITY

Caisson workers have from time to time reported a feeling of increased muscular power while under pressure, and many early investigators of the medical aspects of raised atmospheric pressure have stated that work is easier and less fatiguing and that muscular contractions are stronger. These claims are not substantiated by the experiments of Zenoni (*244*) 1897 who measured the voluntary work done by human subjects in a pressure chamber at a pressure of 2 atmospheres (absolute). No change was found in the work done or the strength of contraction of muscles on artificial stimulation under pressure and there was apparently no change in the capacity of muscles to withstand fatigue. These experiments are suggestive but were not carried out at a pressure sufficiently high to simulate the conditions of the caisson or the working chamber of a tunnel excavation.

244. Zenoni, C. Recherches expérimentales sur le travail musculaire dans l'air comprimé. *Arch. ital. Biol.*, 1897, *27:* 46–60.

H. CARDIOVASCULAR SYSTEM

von Vivenot (*279*) 1865 reported a study of the physiological changes in the circulation in human subjects exposed to a pressure of 3/7 atmosphere above normal barometric pressure in a pressure chamber. The subjects were taken to maximum pressure in 20 minutes, remained at maximum pressure for 1 hour, and were decompressed to normal in 40 minutes. There was a fall in pulse rate of about 6 beats per minute after the maximum pressure was reached and the pulse was found to be still below the control level after the pressure had returned to normal. Some individuals showed an increase in pulse rate under pressure. The amplitude of the pulse was stated to decrease under increasing pressure. von Vivenot found on direct examination of the retinal blood vessels that they were contracted and anemic in subjects at raised pressure. All changes noted tended to disappear on return to normal pressure.

In human subjects under a pressure of about 240 mm. Hg above normal pressure, Panum (*270*) 1868 found a slight increase in the minute volume of respiration. In dogs subjected to a pressure of ½ atmosphere above normal, there was a fall in pulse rate of about 4 to 20 beats per minute and the arterial blood pressure also fell.

Ducrocq (*253*) 1875 reported a fall in arterial blood pressure, a rise in venous pressure, a reduction or rise in pulse rate, a fall in respiratory rate and a reduction in the rate of blood flow. Jacobson and Lazarus (*262*) 1877 subjected dogs to a pressure of 420 mm. Hg above normal. In some instances, there was a slight rise of aortic pressure and in other cases no change. Zadek (*280*) 1880–81 reported a rise in blood pressure, while de Cyon (*250*) 1882 described a fall in blood pressure in dogs subjected to 3 atmospheres (absolute). The respiratory rate fell but de Cyon found an acceleration of the pulse. In 1883, de Cyon (*251*) reported no change in the blood pressure of rabbits subjected to an atmospheric pressure of 2 atmospheres (absolute). At pressures from 2 to 3 atmospheres (absolute), there was a rapid fall in blood pressure.

von Rózsahegyi (*275*) 1885 took pulse tracings with a Marey's sphygmograph of laborers working under pressure in caissons in which a pressure of 1.48 atmospheres (1,166 mm. Hg) was maintained. In these experiments the

pulse frequency rose slightly over a period of 1½ hours of exposure to high pressure. In the particular caisson concerned, the temperature of the air within the working chamber was 10.9°C., whereas outside the air temperature was 13.8°C. The cubic volume of the caisson was 61.12 cu. m. and 10 workers were in the caisson at any one time. The pump delivered 300.3 cu. m. of compressed air per hour. The air was thus completely changed 3.2 times per hour.

In studies made on workmen laboring in a caisson in connection with the building of a bridge over the Necker River near Stuttgart, Germany, Rembold (*273*) 1895 found that the vital capacity at the end of 6 months of work remained the same or was a little less than at the start. This result differs from that of earlier investigators, particularly those who applied the use of raised atmospheric pressure in the treatment of respiratory diseases, and who claimed that raised atmospheric pressure increased ventilation in diseases such as pulmonary tuberculosis. Although the pulse rate was found to be more rapid in the chamber than on the surface, no change was observed in the pulse rate or in the pulse curve as a result of 6 months' work in caissons. In general, there was no pathological hypertrophy of the heart; only one case was cited.

Increased filling of the chambers of the heart, falling of pulse and respiratory rate and cardiovascular adaptations to raised atmospheric pressure were discussed in 1896 by Edelheit (*254*). Hornung (*261*) 1901 stated that the size of the heart increased with rise of pressure in the lock. There was usually a slight decrease again in cardiac size after the working pressure was reached, although the size of the heart did not return to control value. Usually, the pulse rate increased, according to the author, and then diminished. In some cases, there was an immediate and persistent reduction in pulse rate.

Further studies of raised atmospheric pressure on pulse and blood pressure were carried out by Benczúr and Rausch (*245*) 1932 and reference should also be made to experiments reported by Hill (*258*) in 1899–1900. This latter investigator subjected dogs and cats to a gauge pressure of 30 lb. and found no change in arterial and venous blood pressure. There was an increase in respiratory rate and a fall in the pulse rate.

Camus (*249*) 1903 reported that changes in blood pressure were not directly dependent upon changes of pressure and that there was therefore no danger of sudden blood pressure changes on rapid compression or decompression.

In a survey of the arterial blood pressure of 75 men who had worked in compressed air for 1 month to 5 years, Brooks (*248*) 1907 reported no significant change in the blood pressure before entering the lock, after 1 to 2½ hours' work in the lock and after decompression. The slight increase in blood pressure under conditions of work within the chamber were ascribed more to the work than to the increased pressure. Slight increases in blood pressure were reported by Schöppner (*276*) 1909 in human subjects exposed to a pressure of 350 mm. Hg above normal.

Exposure of human subjects to a pressure of 2 atmospheres (absolute) was reported by Javal (*263*) 1913 to produce a slight but definite increase in the blood pressure. The pulse was reported to undergo irregular variations. Bennett and Smith (*246*) 1934 exposed rats to a barometric pressure of 3,040 mm. Hg for 24 to 31 days. There was pulmonary hypertension with low systemic blood pressure. Sclerosis of the pulmonary arterioles was found, but there were no pathological changes in the systemic circulation.

Shilling, Hawkins, and Hansen (*277*) 1936 investigated the pulse, systolic blood pressure and pulse pressure in a group of 31 men tested at atmospheric pressure and at 2, 4, 6, 7, and 10 atmospheres (absolute) and found a reduction in the standing pulse on increased atmospheric pressure as well as a decrease in the pulse rate after exercise. Both the reclining and standing arterial tensions were lower at raised atmospheric pressure than at one atmosphere, as were the reclining and standing pulse pressures. The Schneider Index score was raised in all subjects at all levels of increased pressure. The cardiac output (minute volume) was decreased by about 1 liter at 6

atmospheres (absolute). Kodama (*264*) 1936–38 reported a rise in blood pressure in rabbits exposed to pressures of 680 mm. Hg, 1,200 mm. Hg, and 2,050 mm. Hg above atmospheric pressure.

Breu (*247*) 1940 recorded the electrocardiogram of 120 caisson workers. In 41 percent of these cases, Breu found electrocardiagraphic evidence of myocardial damage (T-wave changes).

Two papers on the pulmonary circulation at various barometric pressures may be consulted. These are reports by von Rohden (*274*) 1913 and Heger and de Meyer (*257*) 1913.

Hawkins, Shilling, and Hansen (*256*) 1934–35 measured the circulation time by the method of injecting Decholin and timing the interval from the moment of injection to the sensation of bitter taste. It was found that exercise at atmospheric pressure of 6 atmospheres (absolute) gave varying effects on these measurements. Exercise at 6 atmospheres did not stimulate the circulation as it does at normal atmospheric pressure.

Many observers have claimed in the past that decompression sickness was caused by the action of pressure and decompression in producing a redistribution of the circulating blood in the body and specifically that on compression the blood was driven by the pressure from the peripheral vessels into the internal structures—the abdominal and thoracic viscera and the central nervous system. On decompression, according to this theory, the peripheral vessels were again opened and there was congestion of blood within the viscera and the brain and cord, thus producing the symptoms of decompression sickness. Moxon (*266*, *267*) 1881 adhered to this congestion theory. He held that blood was forced into the brain during compression and that at a depth of 90 ft., there was a marked rise in arterial tension. Release of pressure, he stated, causes an unknown and probably very complicated injury to nerve centers. When the circulation of the central nervous system was disturbed, certain areas of the spinal cord were first to show effects. It was for this reason that lower parts of the body were more markedly affected in caisson disease.

It is quite clear from the reports on the effects of raised atmospheric pressure on blood pressure, which have just been cited, that blood pressure changes of a magnitude inferred by Moxon do not follow exposure to raised atmospheric pressures. For a more detailed consideration of the cause of decompression sickness, the reader is referred to the section on etiology.

That raised atmospheric pressures do not drive the blood away from the outer parts of the body was shown in 1835 by Poiseuille (*271*). Poiseuille constructed a small pressure chamber of copper with glass observation ports in which animals could be placed and the pressure raised or lowered by means of a pump. By this method, the capillary circulation in the skin of salamanders, frogs, tadpoles, young rats, and young mice was observed under the microscope. In these animals, it was found that the arterial, capillary, and venous circulation in the skin remained unaffected by pressure changes to 3, 4, 6, or 8 atmospheres (absolute). These results were again reported by Poiseuille (*272*) in 1841. Hill and Macleod (*260*) 1902 reported similar results from exposure to high oxygen pressures and these findings were again published by Hill (*259*) 1905–7. Oliver (*268*, *269*) 1909 also made similar observations.

245. Benczúr, G. and Z. Rausch. A fokozott légnyomásos pneumatikus kamra hatása a vérkeringési szervekre. *Orv. Hetil.*, 1932, *76:* 469–471.

246. Bennett, G. A. and F. J. C. Smith. Pulmonary hypertension in rats living under compressed air conditions. *J. exp. Med.*, 1934, *59:* 181–193.

247. Breu, W. Elektrokardiographische Untersuchungen bei Caissonarbeitern. *Wien. klin. Wschr.*, 1940, *53:* 400–402.

248. Brooks, H. A study of blood pressure in compressed air workers. *Med. Rec., N. Y.*, 1907, *71:* 855–857.

249. Camus, L. Recherches sur l'influence des variations de la pression atmosphérique sur la pression sanguine. *C. R. Soc. Biol. Paris*, 1903, *55:* 790–792.

250. Cyon, E. de. L'action des hautes pressions atmosphériques sur l'organisme animale. *C. R. Acad. Sci., Paris*, 1882, *94:* 494–496. [P]

251. Cyon, E. de. L'action des hautes pressions atmosphériques sur l'organisme animal. *Arch. Anat. Physiol., Lpz.*, (Suppl. Bd. Physiol. Abt.) 1883, pp. 212–239. [P, R]

252. Dikowskij, A. (Zur Frage über den Einfluss des erhöhten atmosphärischen Drucks auf des cardiovasculäre System.) *Klin. Med., Mosk.*, 1935, *13* (6): 831–836.

253. Ducrocq, Georges-François-Olive. *Recherches expérimentales sur l'action physiologique de la respiration d'air comprimé.* Thèse (Méd.) Paris, A. Parent, 1875, 56 pp. [R, B]

254. Edelheit, S. Physikalische Erklärung der Caissonkrankheit. *Ärztl. ZentAnz.*, 1896, *8:* 257–259. [R]

255. Galloro, S. Il lavoro dei palombari. Ricerche sperimentali sulla spirometria, portata respiratoria e pressione sanguigna dopo l'immersione. *Folia med., Napoli*, 1934, *20:* 1183–1201.

256. Hawkins, J. A., C. W. Shilling, and R. A. Hansen. Velocity of blood flow as influenced by exercise and increased air pressure. *Proc. Soc. exp. Biol., N. Y.*, 1934–35, *32:* 457–461. [P, M]

257.* Heger, P. and J. de Meyer. État du coeur et de la circulation pulmonaire aux différentes pressions barométriques. *Ann. Soc. Sci. méd. nat. Brux.*, 1913, *71:* 56–63.

258. Hill, L. The influence of increased atmospheric pressure on the circulation of the blood. (Preliminary Note.) *Proc. roy. Soc.*, 1899–1900, *66:* 478–479. [C, P]

259. Hill, L. Compressed air and its physiological effects. *Not. Proc. roy. Instn*, 1905–07, *18:* 364–376. [P]

260. Hill, L. and J. J. R. Macleod. The influence of high pressure of oxygen on the circulation of the blood. *Proc. roy. Soc.*. 1902, *70:* 454–455. [P]

261. Hornung, [ ]. Herzbefund bei Caissonarbeitern. *Münch. med. Wschr.*, 1901, *48:* 1444–1445.

262. Jacobson, H. and [ ]. Lazarus. Ueber den Einflusz des Aufenthaltes in comprimirter Luft auf den Blutdruck. *Zbl. med. Wiss.*, 1877, *15:* 929–930. [P]

263. Javal, A. Recherche sur la tension artérielle dans l'air comprimé. *C. R. Soc. Biol. Paris*, 1913, *75:* 413–415.

264. Kodama, S. Blood pressure of rabbit under abnormal atmospheric pressure (Experiment by Yukawa-Toraziró.) *Jap. J. med. Sci.*, III. Biophysics, 1936–38, *4:* 82–83 Proc.

265. Kodama, S. On the conductivity of perfusion fluid of frog's heart under abnormal atmospheric pressure. *Tohoku J. exp. Med.*, 1938, *34:* 403–412.

266. Moxon, W. Influence of the circulation upon the nervous system. *Brit. med. J.*, 1881, *1:* 491–499; 546–549; 583–586; 628–632; 672–675.

267. Moxon, W. Influence of the circulation on the nervous system. *Lancet*, 1881, *1:* 487–491; 527–531; 565–568; 607–611; 647–651; 685–689.

268. Oliver, T. The physiology and pathology of work in compressed air. *Lancet*, 1909, *1:* 648. [P]

269. Oliver, T. The physiology and pathology of work in compressed air. *Lancet*, 1909, *1:* 943. [P]

270. Panum, P. L. Untersuchungen über die physiologischen Wirkungen der comprimerten Luft. *Pflüg' Arch. ges. Physiol.*, 1868, *1:* 125–165.

271. Poiseuille, [ ]. Recherches sur les causes du mouvement du sang dans les vaisseaux capillaires. *C. R. Acad. Sci., Paris*, 1835, *1:* 554–560. [C]

272. Poiseuille, [ ]. [Effect of high atmospheric pressures on capillary circulation.] *C. R. Acad. Sci., Paris*, 1841, *13:* 933–934. [C]

273. Rembold, S. Ueber die Wirkung der Caissonarbeit auf den Organismus. *Med. KorrBl. Württemb.*, 1895, *65:* 249–254. [P]

274. Rohden, E. von. Zur Blutzirkulation in der Lunge bei geschlossenem und offenem Thorax und deren Beeinflussung durch Über- und Unterdruck. *Dtsch. Arch. klin. Med.*, 1913, *109:* 383–400.

275. Rózsahegyi, A. von. Ueber das Arbeiten in comprimirter Luft. *Arch. Hyg., Berl.*, 1885, *3:* 526–528, [P]

276. Schöppner, [ ]. Die Veränderungen des Blutdruckes unter Einwirkung der komprimierten Luft. *Münch. med. Wschr.*, 1909, *56:* 1686–1687. [P]

277. Shilling, C. W., J. A. Hawkins, and R. A. Hansen. The influence of increased barometric pressure on the pulse rate and arterial blood pressure. *Nav. med. Bull., Wash.*, 1936, *34:* 39–47. [P, M]

278. Smith, F. J. C. and G. A. Bennett. The pulmonary arterial pressure in normal albino rats and the effect thereon of epinephrine. *J. exp. Med.*, 1934, *59:* 173–180.

279. Vivenot, R. von, Jr. Ueber die Veränderungen im arteriellen Stromgebiete unter dem Einflusse des verstärkten Luftdruckes. *Virchows Arch.*, 1865, *34:* 515–591. [C, P]

280. Zadek, I. Die Messung des Blutdrucks am Menschen mittelst des Basch'schen Apparates. *Z. klin. Med.*, 1880–81, *2:* 509–551. [P]

I. BLOOD

As will be seen by consulting the literature on aviation medicine collected by Hoff and Fulton (*3*) 1942 and Hoff, Hoff, and Fulton (*4*) 1944, exposure to diminished atmospheric pressure or to low oxygen tensions at normal barometric pressure causes a temporary increase in the red blood count. Specifically, oxygen acts as a stimulus to the hematopoietic mechanism in the red bone marrow. It might be expected from a survey of the literature referred to that the action of raised atmospheric pressures would be opposite from that of low pressure and that caisson and tunnel workers, as well as divers, might suffer from a form of anemia. Swiontezki (*305*) 1900 referred to such a "caisson anemia" in laborers

working in a caisson under a pressure of 3 to 4 atmospheres (absolute). The red blood cell count and hemoglobin percentage fell. After leaving the caisson, the red blood cell count returned to normal. If the pressure to which the individual had been exposed did not exceed 2 atmospheres (absolute), the red blood cell count returned to normal within 2 or 3 days. Otherwise, a raised value might persist for 1 to 3 weeks. The hemoglobin value returned more slowly. Diminution in the red blood cell count and in hemoglobin values on exposure to raised atmospheric pressure was also found in rabbits. Swiontezki observed a leucocytosis which disappeared within 2 or 3 days after leaving the caisson.

According to Doyon and Morel (*287*) 1901, rabbits exposed to compressed air for 21 days showed a diminution in the red blood cell count amounting to 200,000 per mm. There was a slight decrease in the hemoglobin content of the blood but no change in the specific gravity. In dogs exposed to pressures of 2 atmospheres, Bornstein (*286*) 1911 reported a fall in the red blood count and in the hemoglobin percentage. There was no change in pigeons similarly exposed. According to Fontaine (*289*) 1927, raised atmospheric pressures increased the hematocrit and there was a decrease in the oxygen capacity of the blood. Izumiyama (*296*) 1928 reported a fall in red blood count and hemoglobin value on exposure to high pressures. A similar finding was also reported by Huszcza (*292*, *293*) 1932 and 1933–34. According to this author, blood viscosity was decreased. Raised pressure was found to diminish the red blood count, hemoglobin value, serum protein, and blood viscosity by Kagiyama (*297*) 1934–36.

According to Zoccoli and Leonardi (*308*) 1934–35, raised atmospheric pressure inhibits the hematopoietic activity of bone marrow and delays regeneration of blood. These authors stated that there is an unequal distribution of red blood cells from the central parts of the body to the periphery in animals exposed to compressed air, the red blood count of heart blood being lower than that of peripheral blood.

Ishihara (*294*) 1938 carried out studies on the influence of raised atmospheric pressure on the blood picture of guinea pigs and claimed a rise in red blood count, as well as an increase in the white blood count. Okuda and Sato (*301*) in 1941 published a study on the effect of exposure of human subjects to a pressure of 3 atmospheres (absolute) in a decompression chamber. The tests were carried out on 5 laboratory workers and 4 "Amas" (Japanese women divers). In the laboratory workers, exposure for 1 hour resulted in a slight fall in red blood cell count and in hemoglobin percentage. The same finding was obtained in the "Amas," although the latter were thoroughly acclimatized to diving without apparatus.

Ishikawa (*295*) 1939–40 exposed rabbits in a pressure chamber to pressures of 60, 85, and 130 lb. gauge pressure. He reported a decrease in blood lactic acid, a rise in blood sugar in direct proportion to the degree and the duration of pressure, a decrease in hemoglobin value, and a diminution in the colloidal osmotic pressure of the blood.

For further studies on the effects of raised atmospheric pressures on the blood, reports by the following authors may be consulted: Aggazzotti and de Niederhäusern (*282*, *283*) 1932; Niederhäusern and Zoccoli (*300*) 1933; Aggazzotti (*281*) 1933; de Niederhäusern (*299*) 1933; Heller, Mager, and von Schrötter (*291*) 1895; Swiątecki (*304*) 1899; Ferrannini (*288*) 1914; Solovtsova (*303*) 1914; Zoccoli and Leonardi (*308*) 1934-35; Tronchetti and Parenti (*306*) 1934; and Shatunov (*302*) 1936.

281. Aggazzotti, A. Azione dell'aria compressa sugli animali. VIII. Il tempo di coagulazione del sangue. *Boll. Soc. ital. Biol. sper.*, 1933, *8:* 180–183. [P]

282. Aggazzotti, A. and A. de Niederhäusern. Azione dell'aria compressa sugli animali. II. Modificazioni del tasso glicemico nei mammiferi. *Boll. Soc. ital. Biol. sper.*, 1932, *7:* 1255–1258. [P]

283. Aggazzotti, A. and [ ]. de Niederhäusern. Azione dell'aria compressa sugli animali. III. Modificazioni del tasso glicemico negli uccelli. *Boll. Soc. ital. Biol. sper.*, 1932, *7:* 1259–1261. [P]

284. Aron, E. Ueber die Einwirkung verdichteter und verdünnter Luft auf den intratrachealen Druck beim Menschen. *Virchows Arch.*, 1892, *130:* 297–306, 1 pl. [P]

285. Aron, E. Ueber die Einwirkung barometrisch verschiedener Luftarten auf den intrapleuralen und den Blutdruck bei Kaninchen. *Virchows Arch.*, 1896, *143:* 399–412. [P]

286. Bornstein, A. Über den Einfluss der komprimierten Luft auf die Blutbildung. *Pflüg. Arch. ges. Physiol.*, 1911, *138:* 609–616. [P]

287. Doyon, [ ]. and [ ]. Morel. Action de la pression sur la composition du sang. *Lyon méd.*, 1901, *97:* 65–66.

288. Ferrannini, L. Le alterazioni del sangue per effetto delle variazoni della pressione atmosferica. *Rif. med.* 1914, *30:* 182–186. [R]

289. Fontaine, M. Influence des fortes pressions sur le volume globulaire. *C. R. Soc. Biol. Paris*, 1927, *97:* 1656–1657.

290. Gambigliani Zoccoli, A. and M. Leonardi. Azione dell'aria compressa sugli animali. XVI. Influenza dell'aria compressa sulla rigenerazione del sangue e sul comportamento del quadro ematico di animali salassati. *Boll. Soc. ital. Biol. sper.*, 1934, *9:* 533–534.

291. Heller, R., W. Mager, and H. von Schrötter. Untersuchungen des Hämoglobingehalts und des spec. Gewichts an hundert gesunden Männern. *Z. klin. Med.*, 1895, *28:* 586. [C, P]

292. Huszcza, A. Odczyny biologiczne krwi na zmiany ciśniena atmosferycznego. (Réactions biologiques du sang contre les changements de la pression atmosphérique.) *Lek. wojsk.*, 1932, *20:* 425–436; 501–512; 588–601. (With French and English summaries.)

293. Huszcza, A. Die biologischen Reaktionen des Blutes bei Änderungen des atmosphärischen Druckes. *Acta aerophysiol.*, 1933–34, *1*(1): 82–83.

294. Ishihara, A. Über den Einfluss des gesteigerten Luftdrucks auf das Blutbild des Meerschweinchens. *J. Chosen med. Ass.*, 1938, *28*(9): (Japanese text pagination), 1372–1377; (English text pagination), 66. (In Japanese with German summary.)

295. Ishikawa, T. Studien über die Veränderungen des intermediären Kohlehydratstoffwechsels und des Bluteiweisses bei Überdruckatmung. *Tohoku J. exp. Med.*, 1939–40, *37:* 1–32.

296. Izumiyama, K. Über den Einfluss der Luftdruckveränderungen auf die Zusammensetzung des Blutes. II. Mitteilung. Über- und Unterdruckatmung bei Tieren. (Verhältnis zwischen Blutzusammensetzung und Atemtypus). *Tohoku J. exp. Med.*, 1928, *11:* 374–406.

297. Kagiyama, S. Respiratory and circulatory change in high pressure chamber. *Jap. J. med. Sci.*, III. Biophysics, 1934–36, *3:* 252 Proc.

298. Liebig, G. von. Ein Apparat zu Erklärung der Wirkung des Luftdruckes auf die Athmung. *Arch. Anat. Physiol., Lpz.*, (Physiol. Abt.), 1879, pp. 284–299. [P]

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300. Niederhäusern, A. and A. Gambigliani Zoccoli. Azione dell'aria compressa sugli animali. V. Modificazione del quadro amatico. *Boll. Soc. ital. Biol. sper.*, 1933, *8:* 77–81. [P]

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303. Solovtsova, A. S. [Effect of caisson work on the blood.] *Russk. Vrach.*, 1914, *13:* 483–487; 511–512; 616–618; 794–797; 823–827. [P]

304. Swiątecki, J. Niedokrwistość kesonowa. *Gaz. lek.*, 1899, Ser. 2, *19:* 399–404; 431–438.

305. Swiontezki, J. O. Ueber Caissonanaemie. *St Petersb. med. Wschr.* (*Z*), 1900, neue Folge, *17* (Rev. Russ. med. Z. no. 1): 3. [P]

306. Tronchetti, F. and [ ]. Parenti. La malattia dei cassoni ed altri effetti dell'aria compressa sull'uomo e sugli animali. *Fisiol. e. Med.*, 1934, *5:* 609–621.

307. Vivenot, R. von, Jr. De l'influence de la compression et de la raréfaction de l'air sur les actes mécaniques et chimiques de la respiration. *Gaz. méd. Paris*, 1868, Sér. 3, *23:* 330–332; 342–344; 389–392; 420–422. [P]

308. Zoccoli, A. G. and M. Leonardi. Azione dell'aria compressa sulla rigenerazione del sangue e sul comportamento del quadro ematico negli animali salassati. *Arch Fisiol.*, 1934–35, *34:* 168–188.

J. RESPIRATION

von Vivenot (*332*) 1865 exposed human subjects to pressures of 1 3/7 atmospheres (absolute). At these moderately increased atmospheric pressures, the diaphragm was found to be lowered by 1½ to 2 cm. There was some mechanical dilatation of the lungs according to von Vivenot and this author claimed that the vital capacity was increased by 95 to 130 cc. after 1 hour. Daily exposure to increased atmospheric pressure was reported to produce a permanent increase in lung capacity of about 700 cc. This claim has been made by nearly all the investigators interested in the use of raised atmospheric pressures for therapeutic purposes but many recent studies have failed to confirm any sig-

nificant change in vital capacity. von Vivenot reported a fall in the rate of respiration which he claimed persisted after the subjects left the chamber. The depth of inspiration increased under the influence of raised atmospheric pressure and there was also an increase in the output of carbon dioxide. von Liebig (*298*) 1879 also conducted experiments on human subjects in a pressure chamber raised to moderately increased atmospheric pressures. At a pressure of 1,040 mm. Hg respiration was slowed.

Aron (*284*) 1892, subjected two tracheotomized patients to a pressure of 1½ atmospheres (absolute) in a compression chamber. There was an initial increase in depth of respiration but after 10 to 15 minutes, breathing returned almost to normal. Aron (*285*) 1896 also placed rabbits in a pressure chamber at a pressure of 1½ atmospheres (absolute). In some animals, there was a reduction in the rate of respiration and the intrapleural pressure was changed from minus 3.2 mm. Hg to minus 5 mm. Hg.

Wengler (*333*) 1904–5 reported that an increased pressure of 350 mm. Hg above normal atmospheric pressure resulted in a decrease in body volume of approximately 250 cc. The vital capacity was determined by a spirometer and was stated to be increased by about 200 cc. According to Anthony (*310*) 1927, subjecting human subjects to a pressure of 1.5 atmospheres (absolute) in a pressure chamber for 1 to 1½ hours resulted in an increase in respiratory rate but no change in vital capacity in healthy subjects.

In tests carried out on 25 experienced divers, Shilling, Hansen, and Hawkins (*331*) 1935 found that the vital capacity was increased in all but 1 subject when taken from normal atmospheric pressure to a level of 6 atmospheres (absolute). This increase in vital capacity was, however, not great, the average at normal atmospheric pressure being 4.8 liters and at 6 atmospheres, 5.1 liters. The expiratory force increased in 22 subjects, remained constant in 1 individual and decreased in 2. The average at 1 atmosphere was 172.6 mm. Hg and at 6 atmospheres 199.2 mm. Hg. All subjects showed an increase in breath holding time, the average at atmospheric pressure being 91.0 seconds and at 6 atmospheres, 216.5 seconds.

For further studies on the effects of raised atmospheric pressure on respiration, reference may be made to reports by von Liebig (*323*, *325*) 1869 and 1889, Lenzi (*320*, *321*, *322*) 1933 and 1936, and Anthony (*311*) 1935–36.

According to Aron (*312*) 1902, raised atmospheric pressure changes the volume of intestinal gas with a resulting alteration in thoracic volume and intrapleural pressure. Camis and Lorenzani (*316*) 1932 and Camis (*315*) 1934 also reported an increase in intrapleural pressure as a result of exposure to raised atmospheric pressure. These workers ascribed the change to an effect on the diaphragm. Changes in intrapleural pressure resulting from alterations in barometric pressure were also reported by Aggazzotti and Lenzi (*309*) 1933, Mazzetti (*326*) 1935, and Musini (*327*) 1935.

Many claims were made in the 19th century that exposure to moderately raised atmospheric pressures in therapeutic pressure chambers favorably altered gaseous exchange. For example, von Vivenot (*332*) 1865 stated that exposure of human subjects to a pressure of 1 3/7 atmospheres (absolute) for 2 hours daily resulted in an increase in the carbon dioxide output of about 20 percent, as well as an increase in vital capacity. It was also claimed that urea excretion was increased. Hill and Macleod (*319*) 1903 found that exposure of mice to an air pressure of 5 atmospheres (absolute) for 100 minutes at a time caused a fall of 5 to 10 percent in the carbon dioxide output. At higher pressures, the carbon dioxide output fell as much as 30 percent.

Greenwood (*317*) 1906 and others have shown that as the pressure rises, the percentage of alveolar carbon dioxide falls, so that the total amount of carbon dioxide in the alveoli remains the same. Greenwood gave figures illustrating this point on 2 subjects taken to a pressure of 75 lb. in a pressure chamber.

Scheidin and Farfel (*330*) 1930 conducted experiments on 17 student divers in the Diving School at Leningrad. They reported that

the carbon dioxide excretion was 2 to 25 times as great when resting at the bottom as when resting at sea level.

In experiments carried out by Bean (*313*) 1945, anesthetized dogs were taken to air pressures of a little over 5.5 atmospheres in 1.5 to 3.5 minutes. In 21 out of 22 tests conducted on 4 animals, the carbon dioxide tension in the lungs just after cessation of compression was 10 to 85 percent higher than before exposure to pressure. This increase in the carbon dioxide tension was considered by Bean to be due possibly to compressional flow of air into the lungs preventing exhalation of alveolar air during compression. The compressional flow, according to Bean, also tends to compress the alveolar air, thus temporarily elevating the carbon dioxide tension of the gas in immediate contact with alveolar walls. It was concluded that the carbon dioxide thus dammed back in the blood and tissues constitutes an important etiological factor in the reactions occurring in highly compressed air, especially in the early stages, and which have been attributed by some authors to the narcotic action of nitrogen.

For further general considerations of the effect of raised atmospheric pressure upon respiration, papers by von Liebig (*324*) 1875, Neudörfer (*328*) 1895, and Parodi (*329*) 1938 may be consulted.

309. Aggazzotti, A. and M. D. Lenzi. Azione dell'aria compressa sugli animali. IX. Modificazioni della pressione endopleurica. *Boll. Soc. ital. Biol. sper.*, 1933, *8:* 1306–1308. [P]

310. Anthony, A. Untersuchungen über die Atmung bei erhöhtem Luftdruck. *Beitr. Klin. Tuberk.*, 1927, *66:* 340–365.

311. Anthony, A. J. Die Bestimmung der Lungenventilation bei verschiedenem Luftdruck. *Beitr. Klin. Tuberk.*, 1935–36, *87:* 698–702.

312. Aron, E. Zur Ursache der Einwirkung verdichteter und verdünnter Luft auf den Thierkörper. *Virchows Arch.*, 1902, *170:* 264–284. [P]

313. Bean, J. W. Changes in alveolar CO_2 tension resulting from compression. *Fed. Proc. Amer. Soc. exp. Biol.*, 1945, *4:* 6. [M]

314. Bucciardi, G., M. Leonardi, and E. Ferrarini. Azione dell'aria compressa sugli animali. XV. Ossigeno ed anidride carbonica nell'aria espirata del coniglio sottoposto all'azione dell'aria compressa. *Boll. Soc. ital. Biol. sper.*, 1935, *10:* 787–788.

315. Camis, M. Pression intrapleurale et pression atmosphérique. *Arch. ital. Biol.*, 1934, *91:* 185–190.

316. Camis, M. and G. Lorenzani. Osservasioni sulla pressione endopleurica in svariate condizioni barometriche. *Ateneo parmense*, 1932, *4:* 681–690.

317. Greenwood, M. The influence of increased barometric pressure on man. *Brit. med. J.*, 1906, *1:* 912–914. [P]

318. Harris, J. A. Note on the relationship between barometric pressure and carbon-dioxide excretion in man. *Biochem. Bull.*, 1912–13, *2:* 530–531. Abstr: *Chem. Abstr.*, 1913, *7:* 3999.

319. Hill, L. and J. J. R. Macleod. The influence of compressed air on the respiratory exchange. *J. Physiol.*, 1903, *29:* 492–510. [P]

320. Lenzi, M. Azione dell'aria compressa sugli animali. X. Frequenza e forma del respiro. *Boll. Soc. ital. Biol. sper.*, 1933, *8:* 1308–1310.

321. Lenzi, M. Azione dell'aria compressa sugli animali. XI. Effetti sul pneumotorace unilaterale e bilaterale. *Boll. Soc. ital. Biol. sper.*, 1933, *8:* 1310–1312.

322. Lenzi, M. Azione delle alte pressioni ambientali sulla respirazione. *Riv. Pat. Clin. Tuberc.*, 1936, *10:* 543–567.

323. Liebig, G. von. Ueber das Athmen unter erhöhtem Luftdruck. *Z. Biol.*, 1869, *5:* 1–27. [P]

324. Liebig, G. von. Ueber die Sauerstoffaufnahme in den Lungen bei gewöhnlichem und erhöhtem Luftdruck. *Pflüg. Arch. ges. Physiol.*, 1875, *10:* 479–536. [P]

325. Liebig, G. von. Beobachtungen über das Athmen unter dem erhöhten Luftdruck. *Arch. Anat. Physiol., Lpz.* (Suppl. Bd. Physiol. Abt.), 1889, pp. 41–90. [P]

326. Mazzetti, M. Variazioni delle pressioni endopleuriche in rapporto all'altezza barometrica. *Riv. Pat. Clin. Tuberc.*, 1935, *9:* 592–610.

327. Musini, G. Comportamento della pressione endopleurica con e senza pneumotorace in rapporto alle variazioni barometriche. (Ricerche cliniche e superimentali.) *G. Clin. med.*, 1935, *16:* 583–604.

328.* Neudörfer, [ ]. Das Athmen in der Ebene, in bedeutenden Höhen, in grossen Tiefen und in manchen Krankheiten. *Öst.-ung. BadeZtg.*, 1895, *24:* 97; 105; 113; 123; 129; 137; 145; 153; 161; 169.

329. Parodi, F. Les effets physiques et physiologiques de la pression barométrique sur le poumon. *Rev. Path. comp.*, 1938, *38:* 688–708.

330. Scheidin, J. and M. Farfel. (Zur Frage des Gaswechsels bei den Tauchern.) *Gigiena Truda*, 1930, *8*(12): 15–17. (With German summary.) [M]

331. Shilling, C. W., R. A. Hansen, and J. A. Hawkins. The effect of increased air pressure on vital capacity, expiratory force and breath-holding ability. *Amer. J. Physiol.*, 1935, *110:* 616–619. [P]

332. Vivenot, R. von, Jr. Ueber den Einfluss des verstärkten und verminderten Luftdruckes auf den Mechanismus und Chemismus der Respiration. *Med. Jb., Wien*, 1865, *9:* 205–226. [P]

333. Wengler, J. Aenderung des Körpervolumens bei Auftenthalt in verdichteter Luft. *Pflüg. Arch. ges. Physiol.*, 1904–05, *106:* 313–322.

334. Anon. Luft-tryckets eller barometerståndets inflytande på allmänbefinnandet och på vissa sjukdomar. *Upsala LäkFören. Förh.*, 1867–68, *3:* 403–406.

K. BLOOD GASES

Paul Bert (*336, 337*) 1875 found that the amount of oxyhemoglobin in the blood was not increased by raised pressures. Hill and Macleod (*338*) 1903 exposed animals to a pressure up to 100 lb. They found that added nitrogen and oxygen are dissolved according to Dalton's law, but that solution is slow, and therefore the maximum gas concentration was attained only after more than 1 hour at the given pressure. It was stated that the concentration of carbon dioxide in the blood was diminished under high oxygen pressures.

335. Bert, P. Sur la capacité du sang pour l'oxygène aux diverses pressions barométriques. *C. R. Soc. Biol. Paris*, 1873, Sér. 5, *5:* 372. [P]

336. Bert, [ ]. Capacité du sang pour l'oxygène aux diverses pressions barométriques. *Gaz. hebd. Méd. Chir.*, 1875, *12:* 188. [P]

337. Bert, P. De la quantité d'oxygène que peut absorber le sang aux diverses pressions barométriques. *Gaz. hebd. Méd. Chir.*, 1875, *12:* 214–215. [P]

338. Hill, L., and J. J. R. Macleod. The influence of compressed air and oxygen on the gases of the blood. *J. Physiol.*, 1903, *29:* 382–387. [P]

L. METABOLISM

von Vivenot (*343*) 1866 reported that the average body temperature varied by only a fraction of a degree (Reamour) in rabbits exposed to moderately raised atmospheric pressures. In goats, there was a slight increase in body temperature during the maximum application of raised atmospheric pressure with a fall to a fraction of a degree below normal as pressure was released. von Vivenot was unable to substantiate the claims of various workers that increased pressure caused a feeling of warmth. According to Fraenkel (*341*) 1881, dogs exposed to 2 to 3 atmospheres (absolute) showed no increase in blood carbon dioxide and animals subjected to a pressure of 2 atmospheres (absolute) for 5 hours a day for several days showed no change in nitrogenous excretion.

339. Aggazzotti, A. Azione dell'aria compressa sugli animali. XVII. La combustione dell'alcool etilico iniettato nei ratti. *Boll. Soc. ital. Biol. sper.*, 1935, *10:* 782–784. [P]

340. Aggazzotti, A. Azione dell'aria compressa sugli animali. XVIII. Combustione dell'alcool etilico iniettato in dosi crescenti. *Boll. Soc. ital. Biol. sper.*, 1935, *10:* 784–786. [P]

341. Fraenkel, A. Ueber den Einfluss der verdichteten und verdünnten Luft auf den Stoffwechsel. *Z. klin. Med.*, 1881, *2:* 56–78. [P]

342. Sarre, H. Untersuchungen über Beziehungen zwischen Hochdruck, Nebennierenrindenhormon und Kochsalz. *Dtsch. Arch. klin, Med.*, 1944, *192:* 167–181. [P]

343. Vivenot, R. von. Ueber die Veränderung der Körperwärme unter dem Einfluss des verstärkten Luftdruckes. *Med. Jb., Wien*, 1866, *11:* 113–146. [P]

M. FERMENTATION

Paul Bert (*344, 346, 347*) 1875 and 1876 exposed a piece of muscle to an oxygen tension corresponding to 23 atmospheres of air for 5 days. The meat was not putrid at the end of the experiment. In a further experiment, muscle was exposed to an oxygen tension corresponding to 44 atmospheres of air (80 percent oxygen at 10 atmospheres). In this case, also, there was no putrefaction at the end of 21 days. The activity of enzymes such as diastase, pepsin, etc., was not interfered with by these pressures. Bert (*345*) 1875 distinguished between "organic" ferments which were destroyed by the action of compressed air and "unorganized" ferments such as diastase which were not destroyed.

344. Bert, [ ]. Action de l'air comprimé sur les ferments vivants et les ferments inorganisés. *Gaz. hebd. Méd. Chir.*, 1875, *12:* 60. [C, P]

345. Bert, [ ]. Action de l'air comprimé sur les ferments. *Gaz. hebd. Méd. Chir.*, 1875, *12:* 79. [C, P]

346. Bert, P. Influence de l'air comprimé sur les fermentations. *Gaz. hebd. Méd. Chir.*, 1875, *12:* 437. [C, P]

347. Bert, P. Influence de l'air comprimé sur les fermentations. *Ann. Chim. (Phys.)*, 1876, Sér. 5, *7:* 145–155. [C, P]

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N. URINARY SECRETION

For a review of the early observations on the effect of raised atmospheric pressures on urinary secretion, the reader is referred to a paper by Hadra (*348*) 1879. Paul Bert (*16*) 1878 concluded that compressed air resulted in an increase in urea production and many observers of the effect of moderately increased atmospheric pressures on patients in therapeutic pressure chambers held that there was an increase in urine volume as well as total urinary solids. Hadra exposed human subjects to a pressure of 2 atmospheres (absolute) for 3 to 4 hours per day, and in opposition to a number of previous observers, was able to detect no objective increase in urine volume. Careful measurements of urea output indicated no significant increase in urea excretion. Hadra's report may be consulted for actual figures.

A review of the effects of high pressures on urine and urea production was published as a medical thesis in 1889 by Orthmann (*349*) and this monograph should be consulted by those wishing to be familiar with the developmental aspects of this subject.

348. Hadra, S. Die Einwirkung der comprimirten Luft auf den Harnstoffgehalt beim Menschen. *Z. klin. Med.*, 1879, *1:* 109–130. [C, P]

349. Orthmann, C. *Ueber den Einfluss der comprimierten Luft auf die Harnstoffproduktion.* Inaug.-Diss. (Med.) Halle, Heynemann'sche Buchdruckerei (F. Beyer), 1889, 33 pp. [R]

O. TISSUE GASES

Campbell and Hill (*350*) 1923–24 reported on the effects of barometric pressure on the oxygen and carbon dioxide tension in the air between the skin and the muscles. It was found that there was a decrease in the percentage of carbon dioxide and an increase in the percentage of oxygen in the subcutaneous tissues.

350. Campbell, A. and L. Hill. The effect of barometric pressure on the O_2 and CO_2 tension in air between the skin and the muscles. *J. Physiol.*, 1923–24, *58:* xxv-xxvi. [C, P]

P. ABDOMINAL PRESSURE

In caisson workers in the chamber, there is a diminution in the volume of intestinal gases and a general reduction in the size of the abdomen. Abdominal pressure falls. For a study of the effects of compression and decompression on abdominal pressure in animals, reference may be made to a report by Aggazzotti (*351*) published in 1932.

351. Aggazzotti, A. Azione dell'aria compressa sugli animali. I. Modificazioni della pressione abdominale durante la compressione e la decompressione. *Boll. Soc. ital. Biol. sper.*, 1932, *7:* 885–888. [P]

Q. SYNOVIAL SECRETION

The 19th century observers of the effects of moderately increased barometric pressures used as a therapeutic method reported an increase in various body secretions. For instance, it was believed that the production of saliva and digestive juices was increased and that there was a raised output of urine by the kidneys. Increased barometric pressure was also held to augment secretions from synovial surfaces. Such an effect was reported, for example, by Guérin (*352*) in 1840.

352. Guérin, J. Mémoire sur l'intervention de la pression atmosphérique dans le mécanisme des exhalations séreuses. *Gaz. méd. Paris*, 1840, Sér. 2, *8:* 321–329. [C]

II. PHYSIOLOGICAL EFFECTS OF DECOMPRESSION FROM PRESSURES HIGHER THAN ONE ATMOSPHERE

A. GENERAL STUDIES OF THE EFFECTS OF DECOMPRESSION

That decompression of the atmosphere surrounding animals may lead to bubble formation in the blood and tissues was observed by Boyle (*2564, 2565*) 1670 and van Musschenbroek (*56*) 1739 and this observation has been repeatedly made by many other investigators since that time. However, some experimenters were unable to extract gases from tissues on decompression. For example, Davy (*360*) 1829 obtained no gas from blood, milk, or tissues on subjecting them to decompression with a vacuum pump.

Bert (*355*) 1873 observed that animals, decompressed rapidly from a pressure of 7 atmospheres, could be saved by inhalation of pure oxygen. Gases were released from the body fluids by decompression. Foam was

found in the right auricle at autopsy and it was believed that these bubbles tended to interfere with the circulation. Bert held that the paralysis resulting from repeated decompression from high pressures was due to the presence of gas bubbles in the central nervous system and that slow decompression prevented bubble formation and its sequelae. Bert stated that breathing oxygen acted by hastening the absorption of nitrogen bubbles, and he recommended that oxygen be breathed by divers or compressed air workers after decompression. Bert (*354*) 1873 also subjected dogs to explosive decompression from a pressure of 7 atmospheres to normal pressure. Gases were found in the tissues, in the peritoneal cavity, in the spinal cord, and in the fluids of the eye. Rapid decompression from pressures above 7 atmospheres was usually fatal. However, one very thin, spare little dog survived rapid decompression from pressures of 8½, 8, and 7¾ atmospheres. No gas was found in blood drawn from the veins in this animal after each decompression. In the laboratory, this dog was fattened up and later died when decompressed rapidly from 8 atmospheres. It appeared to Paul Bert that increased body fat lowered the tolerance of the organism to decompression. Bert also found that birds were not killed by decompression from pressures as high as 12 atmospheres and speculated on the possible reason for these species and individual differences in tolerance.

For further studies on rapid decompression from high pressures and the formation of gas bubbles in the blood, a paper published by Bert (*356*) in 1875 should be consulted.

Phillipon (*370*) 1892 reviewed Bert's investigations of the effects of sudden decompression on laboratory animals. Phillipon decompressed a rabbit instantaneously from a pressure of 5¼ atmospheres. Death occurred within 1 minute of decompression and at autopsy, the blood vessels were found to be filled with free gas. Another rabbit survived rapid decompression from 3½ atmospheres and when sacrificed and examined showed gas bubbles in the vascular system. Phillipon found that rabbits were unable to survive decompression from pressures higher than 3½ atmospheres and considered that death was due to the mechanical action of bubbles in the blood vessels. Heller, Mager, and von Schrötter (*363*) 1897 also carried out experimental investigations of the action of rapid changes of air pressure on the organism. This report and their monograph (*28*) published in 1900 should be consulted for studies on the nitrogen, oxygen, and carbon dioxide content of free gas bubbles in the blood of decompressed animals. Heller, Mager, and von Schrötter's studies have been reviewed by von Cyon (*359*) 1897-98, who also reported effects of raised atmospheric pressure on respiratory rate, pulse, and blood pressure.

Hill (*365*) 1905 concluded that oxygen or raised atmospheric pressures did not increase the metabolic rate and that oxygen could not be used as an agent for increasing tissue combustion above normal levels. Studies were also reported of the absorption of nitrogen by the blood. At 1 atmosphere, 100 cc. of blood absorbed 1.2 cc. of nitrogen; at 4 atmospheres (absolute), 4.92 cc. of nitrogen were absorbed. On decompression from 4 atmospheres to 1 atmosphere, 100 cc. of blood gave up 3.69 cc. of nitrogen. Hill calculated that the whole blood of a 70 kg. man would release about 130 cc. of nitrogen and the tissues approximately 10 times that much. Gas recovered from the right heart of a dog decompressed from high pressures was analyzed and found to contain 82.8 percent nitrogen, 15.2 percent carbon dioxide, and 2.0 percent oxygen.

In decompression experiments carried out on rats, mice, cats, and rabbits, Hill and Greenwood (*368*) 1907-8 found that small animals were relatively immune to decompression sickness, but that if the circulation is slowed by chloroform administration, this relative immunity disappears. Age has some effect on tolerance to decompression, according to Hill and Greenwood, but body size appears to be more directly related to susceptibility to caisson disease.

Greenwood (*362*) 1908 referred to the investigations of Bert; Phillipon; and Heller, Mager, and von Schrötter, as well as earlier investigations of Hoppe and Bucquoy. Greenwood

opposed the earlier belief that raised atmospheric pressure accelerated metabolism. The composition of gas in bubbles liberated on decompression was discussed. Greenwood believed that any animal devoid of a circulatory system involving a respiratory system was immune to decompression sickness, even though it might be sensitive to raised oxygen pressures.

Hill (*366*) 1909 decompressed frogs and other animals from high atmospheric pressures while observing the circulation in the peripheral vessels of the web between the toes. There was no change in the circulation during exposure to high pressures and on rapid decompression, bubbles appeared in the circulating blood. On recompression, bubbles tended to redissolve. A controversy regarding the priority of these observations arose between Hill and Oliver and this matter is discussed in the articles cited.

In 1909–10, Hill and Greenwood (*369*) repeated experiments originally carried out by Hoppe. This worker had exposed animals to a partial vacuum and discovered gas bubbles in the circulatory system. Hill and Greenwood decompressed a rabbit from 1 atmosphere to a pressure of 50 mm. Hg within a period of 3 minutes. At this pressure, the rabbit died, and on autopsy, the heart and great vessels were found to contain air. However, no bubbles were seen in mice, guinea pigs, a cat, and a kitten similarly exposed. It therefore appeared, according to Hill and Greenwood, that in larger animals bubbles were more likely to form than in smaller animals.

Gaertner (*361*) 1920 found that mice died very soon after rapid decompression from 10 atmospheres (absolute). The body was swollen, the skin taut, and the heart full almost to bursting with foamy blood. Gaertner accepted the view that caisson disease results from too rapid decompression, releasing nitrogen into the circulatory system. Rapid decompression was considered dangerous only after long periods of compression when the tissues are saturated. The author suggested that inhalation of hydrogen might be used to shorten decompression time. Hydrogen might be useful, he believed, in diluting oxygen as a respiratory gas for divers. However, the danger of explosion with such a gas mixture is certainly an objection to its use.

In 1945, Wagner (*374*) made direct observations of gas bubbles in pial vessels of cats following rapid decompression from high atmospheric pressures. In 14 cats, Forbes windows were placed in the parietal region of the skull and the pial vessels were directly visualized under a magnification of 75 diameters. The animals were subjected to an atmospheric pressure of 75 lb. per sq. in. for 1 hour and then decompressed to normal within 3 to 5 seconds. Twenty minutes after decompression, the cat was removed from the chamber and the pial vessels observed at intervals during a period of 24 hours or until death occurred. In most cases, there was no change in the caliber of the vessels, but in 3 animals an arterial vasoconstriction of approximately 25 to 30 percent was observed. In one case, the veins were greatly dilated and in another there was a moderate contraction. In all animals following decompression, Wagner observed intravascular agglutination of red cells—so-called "sludge" formation. The significance of this clumping of blood cells is not clear, but according to Wagner, "sludge" formation always accompanied reduction in blood flow. Gas bubbles appeared in the pial vessels of some cats and not in others. The bubbles were always manifest first in the arteries and then in the veins. Six cats which died shortly after decompression showed gas bubbles in the right auricle and ventricle as well as the mesenteric vessels and fat. Three cats died several hours after decompression and these showed the same bubble picture as the animals noted above who died a short while after decompression. In 5 cats who were killed 24 hours after decompression, no gross signs of bubble formation were seen anywhere. Wagner concluded that the gas bubbles in the pial vessels occurred as a consequence of passage of air bubbles from the lungs through the heart and into the arterial system. Intravascular agglutination noted by Wagner has been discussed by End (*2548*) 1938 as a possible etiological factor in the production of caisson disease.

This hypothesis was critically discussed by Shilling (*1142*) 1941.

For references to the literature on the physiological effects of decompression to atmospheric pressures below 1 atmosphere, reference should be made to Hoff and Fulton (*3*) 1942 and Hoff, Hoff, and Fulton (*4*) 1944.

Of considerable interest is the effect of decompression on marine animals. Such studies do not strictly come within the field of this Sourcebook. However, reference may be made to a paper by Rabaud and Verrier (*371*) 1932 on the effects of decompression on fish without swim bladders. In these experiments, two soles were decompressed slowly to a pressure of 265 mm. Hg. Bubbles of gas were liberated from the mouth, the opercula, and from the surface of the body. At 165 mm. Hg, the animals became agitated, rose passively to the surface, gave up more bubbles, and fell to the bottom. At 115 mm. Hg, more bubbles were given off, and finally both fish rose to the surface, their abdomens swollen and eyes protruding. It was suggested that the gas probably was liberated from the blood traversing the gills.

Reference may be made to a paper by Schubert and Grüner (*372*) 1939 on the development of free gas in the blood and tissues on rapid decompression. The effect of exercise on the incidence of decompression sickness at altitude has been investigated by Cook, Williams, Lyons, and Lawrence (*358*) 1944. At various simulated altitudes, exercise produced statistically valid increases in the incidence of symptoms of decompression sickness. This finding has been generally confirmed. Early workers observing the effects of decompression on divers and caisson laborers have held that exercise during decompression was of value in preventing symptoms of caisson disease but at present such exercise is not recommended.

For further general studies on the effects of decompression, reference may be made to papers by Boycott and Damant (*357*) 1907-8 and Shaw (*373*) 1936.

353. Bert, [ ]. Phénomènes observés sur un chien qui avait été soumis pendant deux heures à une pression de 10 atmosphères. *Gaz. méd. Paris*, 1873, Sér 4, *28:* 157. [C, P]

354. Bert, [ ]. Sur les effets des modifications de la pression barométrique. *Gaz. méd. Paris*, 1873, Sér. 4 *28:* 386–387. [C, P]

355. Bert, P. Sur l'influence des modifications dans la pression atmosphérique. *C. R. Soc. Biol. Paris*, 1873, Sér. 5, *5:* 27–30. [C, P]

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B. PHYSIOLOGY OF BUBBLE FORMATION

One of the criticisms of the gas embolism theory discussed by Van Rensselaer (*1350*) 1891 was that the quantity of gas liberated as a result of decompression was much less than the theoretical amount. However, Ham and Hill (*376*) 1905-6 found that the amount of gas collected from the bodies of rats decompressed rapidly from 10 to 20 atmospheres was even greater than theoretically expected. It was suggested that animals swallowed air under pressure and that a part of the total gas collected from the bodies of these decompressed rats was the additional amount taken into the alimentary tract.

Quincke (*381*) 1910 carried out experiments on bubble formation in water and body fluids, etc. Water or 0.9 percent saline rapidly gave off bubbles when decompressed from 4 or 5 atmospheres. In serum and albumin solutions, bubbles developed much later and more sparingly. Platinum wire and other foreign bodies were found to facilitate the development of bubbles. Cerebrospinal fluid resembled water and albumin solution in relation to bubble formation. Olive oil and human fat were found to absorb three to five times as much gas (nitrogen and oxygen) as water did. The authors found that small animals such as mice and frogs withstood decompression from 4 or 5 atmospheres without disturbance, while many rats and guinea pigs died after a period of 10 to 20 minutes with air in the heart, arteries, and veins. In decompressed frogs, gas was found in the lymph sacs and in the body cavities as well as in body tissues. The high solubility of nitrogen in fat rendered the body fat a rich nitrogen reservoir. In the spinal cord, for instance, conditions were particularly favorable for bubble formation; the greater predilection for the cord than for the brain was ascribed to the less favorable blood supply of the former.

Twort and Hill (*382*) 1910–11 carried out experiments in which 50 cc. of water were shaken for 30 minutes at a pressure of 90 lb. per sq. in. at room temperature (11.5° to 15° C.) and the barometric pressure then lowered to 20 lb. per sq. in. within 10 to 20 minutes. There were no visible bubbles in the liquid on decompression to 20 lb. per sq. in. even if the water was shaken vigorously. However, bubbles appeared on agitation of the water at 20 lb. per sq. in. and at normal barometric pressure. Twort and Hill, therefore, believed it safe to decompress an individual from a pressure of 90 lb. per sq. in. down to 20 lb. per sq. in. as far as the watery part of the body was concerned. However, as Vernon (*428*) 1907 has shown, nitrogen and oxygen are five times more soluble in fat than in water at 1 atmosphere. This observation was essentially confirmed by Twort and Hill.

The formation of gas bubbles has been investigated by Piccard (*380*) 1941. In his experiments, water was saturated with air at 5 atmospheres and decompressed to normal pressure. There was rapid cavitation and strong effervescence of bubbles. Water saturated with air at 1 atmosphere and decompressed to 0.2 atmospheres showed cavitation and slow, continued release of gas bubbles. Piccard considered that this explained why it was more dangerous to decompress a human subject from 5 atmospheres to normal than from normal pressure to 0.2 atmospheres. Mathematically, Piccard demonstrated that a bubble forms in the first case, i.e., on decompression from 5 atmospheres, when 27,600,000 gas molecules meet, whereas, in the second case, i.e., from 1 atmosphere to 0.2 atmospheres, the bubble forms when 690 million molecules meet. Hence, there is a much greater likelihood of bubble formation when the diver

is decompressed than when the aviator ascends to high altitude.

Harvey, McElroy, Whiteley, Warren, and Pease (*379*) 1944 found that nembutalized cats taken at rest to simulated altitudes of 45,000 to 50,000 ft. rarely developed bubbles, but that if the hind legs were stimulated electrically, bubbles appeared in the post cava even at 35,000 ft. equivalent. If resting nembutalized cats were subjected to an increased atmospheric pressure for several hours and then decompressed to 1 atmosphere, visible bubbles did not appear in the post cava unless the pressure difference (ΔP) was over 2 atmospheres. At a ΔP of 3.5 atmospheres, almost all cats developed bubbles whether resting or stimulated. Bubbles were found to form readily in cats taken to altitude at a ΔP of 0.8 atmospheres plus the pressure difference due to muscular contraction, whereas, at high pressures a ΔP of 2 to 2.5 atmospheres plus the pressure difference due to muscular contraction is necessary.

Whitaker, Blinks, Berg, Twitty, and Harris (*383*) 1945 reported that muscular activity during decompression from high altitudes results in bubble formation in the blood of intact bullfrogs. The amount of gas developed was found to depend upon the degree of muscular activity and the supersaturation as influenced by the altitude. In dissected frogs which were decompressed from simulated altitude, bubbles were found in the veins leading from active muscles but not inactive muscles. Muscular activity in decompressed rats resulted in bubble formation in veins coming from the muscles and often in the lymphatic system. In quiescent rats no bubbles were formed. Violent activity carried out before decompression favored bubble formation during decompression itself. The authors found that preoxygenation for 2 to 4 hours before decompression reduced the incidence of bubble formation in bullfrogs and ascribed this to the removal of the nitrogen. Mechanical agitation and increased metabolic carbon dioxide output were considered predominant factors in the effect of exercise in causing bubble formation.

Harris, Berg, Whitaker, and Twitty (*377*) 1945 subjected bullfrogs to pressures ranging from 3 to 60 lb. per sq. in. Bubble formation was not found after decompression from the above range of pressures except in animals in which muscular activity had occurred. Anesthetized frogs remained bubble free. Rats compressed to pressures of 15 to 45 lb. per sq. in. likewise did not show bubbles unless exercised on return to sea level. However, bubbles formed without voluntary muscular exercise in anesthetized rats previously subjected to 60 lb. per sq. in. The small movements in breathing were believed by the authors to be sufficient to initiate bubbles in the presence of very high supersaturations of nitrogen. With exercise, bubbles appeared in rats previously compressed at 15 lb. per sq. in. and in frogs previously exposed to pressures as low as 3 lb. per sq. in.

For a comprehensive and recent review of bubble formation in blood and tissues as a result of decompression, reference may be made to a paper by Harvey (*378*) 1945. As Harvey stated, if a bottle of soda water under a tension of 3 to 4 atmospheres is left upright and undisturbed for some hours, no bubbles will form if the cap is removed without jarring the bottle. Bubbles will develop on the walls of a glass if the liquid is poured out. Sometimes bubbles arise from a clearly visible dust particle in the bulk of the liquid and sometimes, as Harvey has pointed out, a chain of bubbles may be seen arising from a point where a gas mass remains sticking to the glass. If the tumbler is greasy, the hydrophobic region will be outlined by an abundance of bubbles which persist until the soda water has lost its excess gas. Harvey states that the bubbling and effervescence is due to minute gas masses which stick to the dry walls of the glass, or dust particles which grow into bubbles as soon as the pressure release occurs. This is proven by pouring soda water into a scrupulously clean and wet tumbler. No bubbles form except during the first disturbance of the surface due to pouring. If some dry powder such as infusorial earth is dropped into the quiet soda water, carbon dioxide separates from the liquid with ex-

plosive violence, but if the infusorial earth has first been boiled in water to remove its air film and is then placed while wet into the soda water, not a single bubble will appear. However, a paraffined surface (which is hydrophobic), no matter how well cleaned, will always bubble profusely. Harvey believes that all these effects are due to small gas masses or "gas nuclei" which stick to any dirty and especially greasy surface, but not to clean wet glass. Harvey pointed out that the sticking of gas is a matter of the contact angles. On a surface such as glass, a zero contact angle means that no bubble can stick and no nucleus remains, but with any positive contact angle, nuclei can stick and may be stable under certain conditions.

Harvey also reviewed the effect of local decreases in hydrostatic pressure on bubble formation. As water runs at sufficient velocity through a constriction in a tube, by Bernoulli's law, the pressure decreases at such a narrowed point and cavitation occurs. Harvey doubted whether the flow of blood in the blood stream was anywhere sufficient to produce this effect (Reynold's effect) in areas of constriction in the blood vessels. Harvey showed that bubbles are formed in water at 1 atmosphere if the bottom of a container is hit with a series of blows. Whenever tensions are built up, as when a glass rod immersed in water is suddenly withdrawn, or when a propeller blade by rotation continuously pulls away from the water, cavities may be formed and bubbles appear. If the liquid is already supersaturated with gas and subjected to a blow or to sudden local reduction of tension, the formation of bubbles is greatly facilitated. In the body, one is dealing with surfaces which can be pulled apart and in which local tensions are involved. According to Harvey, cavities may form and into these, gas will move with extraordinary rapidity, leaving a gas bubble when the cavities collapse. That such a mechanism must be involved in the formation of bubbles in the animal is indicated, according to Harvey, by the fact that contracting muscular tissue, for example, is particularly prone to form gas bubbles and that in connective tissue, bubbles form very readily when the tissue is pulled or cut. It is perhaps significant that the "bends" are particularly associated with regions rich in connective tissue.

From the preceding considerations, Harvey believed that the tendency of bubble formation depends upon two factors: (a) the gas tension, and (b) the pressure within the liquid. Thus ΔP (pressure difference) equals t (gas tension) minus P (hydrostatic pressure). If no gas nuclei are present and the fluid is at rest, the ΔP can rise to 1,000 atmospheres without bubbles forming. However, if the surface of the container is pitted or cracked, spontaneous bubbles form at much lower pressure differences. Harvey stated that if carbon dioxide and nitrogen are both dissolved at the same tension in a liquid surrounding the cavity, the gases will diffuse into the cavity at rates depending upon their concentrations rather than their tensions. When the cavity collapses, there will be a much greater proportion of carbon dioxide than of nitrogen in the bubble. Later, the proportions of carbon dioxide and nitrogen will adjust themselves so as to reflect the partial pressures of the gases. Bubbles can be shown to grow in passing through a large layer of liquid saturated with carbon dioxide after passing through an air saturated layer, and Harvey believed that rapid bubble growth may be expected by this mechanism in a contracting muscle where a large amount of carbon dioxide is produced. Later, the composition of the bubble formed in the muscle will be altered by the replacement of carbon dioxide with nitrogen. At altitude, bubbles were rarely observed in resting animals but appeared in the blood vessels as a result of muscular contraction. Harvey and his colleagues found that animals decompressed to 1 atmosphere from high air pressures do exhibit profuse formation of bubbles in blood vessels and many tissues are a froth of bubbles. Harvey concluded that bubbles in the body arise from gas nuclei sticking to or formed on, or within the epithelial linings of the vascular system or extravascular spaces and only when the minute bubbles have enlarged to the point of instability do they pass into the blood stream.

As has been previously stated, nembutalized cats observed for 1 hour at 45,000 ft. rarely showed bubbles in the post cava and even at 50,000 ft., bubbles were not usually seen during a 60-minute observation period. However, if the hind legs of the cat were stimulated vigorously, bubbles from the limb veins were seen moving up the post cava, sometimes within 5 seconds of stimulation. When the hind legs of cats were stimulated once a second for 20 seconds and the animals then taken immediately to a simulated altitude of 25,000 ft., bubbles appeared in 7 out of 10 cats. However, if there was a wait of 10 minutes before ascent to 45,000 ft., bubbles appeared in only 2 out of 10 cats. During this wait, the enlarged gas nuclei in the animals had presumably returned to their original condition. Therefore, Harvey believed that vigorous exercise should not be carried out just before ascent. In the conception of the bubble formation mechanism during muscular contraction advanced by Harvey, both carbon dioxide concentration and mechanical tension within the muscle are emphasized. However, Harvey believed that the facts appear to point to mechanical tension as being the more important of these two factors. The bubbles formed in the blood are mainly composed of nitrogen, but when very small and first formed, undoubtedly contain a high concentration of carbon dioxide as well, according to Harvey. This excess carbon dioxide must pass out of the bubble again. Thus, in the early growth of a gas nucleus, carbon dioxide may play an important role, according to Harvey's concept, but for bubble persistence, the nitrogen tension is the determining factor.

In regard to the site of bubble formation in animals, Harvey found bubbles in all regions of the body of a cat after extreme compressed air treatment. There were bubbles in the arteries, viens, and lymph vessels as well as the humors of the eye and the amniotic fluid although not in the bladder urine. Gas was very abundant in fatty tissue and could be seen in veins draining fat deposits. Harvey had not seen whether bubbles occurred within cells of the body, but he regarded this as unlikely. All attempts to demonstrate bubble formation within living single-celled organisms such as paramecia or amebae or in sea urchin or star fish eggs failed. In some experiments, the cells were subjected to a pressure as high as 2,300 lb. per sq. in. before decompression. In cats taken to a simulated altitude of 45,000 ft., bubbles appeared mostly in the veins while some were found in lymph vessels; they were not seen in the eye humors, the urine, amniotic fluid, or around joints. However, in these experiments, the examination for bubbles could not be made at altitude, and at ground level the gas may have contracted sufficiently to escape detection.

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C. NITROGEN SATURATION AND DESATURATION

Whatever the etiology of caisson disease, changes in atmospheric pressure do produce alterations, sometimes sudden, in the volume of gases dissolved in the blood. On decompression, these gases, particularly nitrogen, may be

unloaded from the blood and tissues in the form of macroscopic bubbles.

In 1892, Jolyet and Sigalas (*408*) determined that nitrogen and hydrogen have the same solubility in serum. Increasing the number of blood cells was reported to increase the amount of gas taken up by the blood and this was taken by the authors as indicating that gas was adsorbed onto blood cells. Bohr (*388*) 1897 determined that dog or beef blood, or pure hemoglobin, in solution will take up 0.43 to 0.66 cc. more nitrogen per 100 cc. of fluid than an equivalent volume of water. This increased absorption was believed to occur only in the presence of oxygen. In 1905, Bohr (*389*) also determined the absorption coefficient of hydrogen, oxygen, nitrogen, and carbon dioxide in water, blood, and plasma. Similarly, Just (*409*) 1901 reported on the solubility of nitrogen, carbon dioxide, hydrogen, and carbon monoxide in various organic solutions.

In 1907, Vernon (*427*) published studies on the solubility of air in fats and its relation to caisson disease. The fats used were olive oil, cod-liver oil, and lard. The oils were saturated by shaking vigorously with air for several minutes at 15° C. and at 37° C. The samples were then allowed to stand until the excess air had risen to the top. The weighed samples were then digested with sulfuric acid and the liberated gases were collected and analyzed. Vernon found that the following volumes of gas were dissolved in 100 cc. of oil or lard:

	Olive oil		Cod-liver oil		Lard
	15° C.	37° C.	15° C.	37° C.	45° C.
	cc.	*cc.*	*cc.*	*cc.*	*cc.*
Oxygen	2.28	2.33	2.29	2.22	2.33
Nitrogen	5.26	5.19	5.06	5.08	5.11
Carbon dioxide	0.20	0.16	0.21	0.21	0.13

Previous studies showed that 100 cc. of water at 15° C. contained 0.733 cc. of oxygen and 1.41 cc. of nitrogen. Plasma dissolved 2.5 percent less nitrogen than water. Vernon concluded that at body temperature the fat of mammals dissolves at least 5 times as much nitrogen as water or blood and blood plasma.

Hill and Greenwood (*406*) 1907 estimated the degree of nitrogen saturation of the body by determination of the nitrogen saturation of urine at various stages of compression and decompression. At pressures of 30 to 45 lb. per sq. in., saturation was reached, according to Hill and Greenwood, in 10 to 15 minutes. The authors admitted that saturation of the kidneys is probably more rapid than that of other tissues. Greenwood (*401*) 1907 reported that a decompression rate as slow as 20 minutes per atmosphere was not slow enough to allow for complete nitrogen desaturation and some excess of nitrogen was found present in the urine 30 minutes after decompression (Greenwood (*402*) 1908).

Hill, Twort, and Walker (*407*) 1910–11 compressed a human subject to a pressure of 45 lb. per sq. in. at which pressure he remained for 1 hour. The urine was collected every 7 minutes during the experiment and the subject drank a quart of water one-half way through the compression period. The percentage of nitrogen in each sample of urine was measured. It was found that nitrogen does not reach equilibrium with the atmospheric pressure in less than 10 to 15 minutes. The authors contested the validity of the Admiralty decompression tables. They reported that breathing oxygen helped clear the body of nitrogen.

A summary of investigations of nitrogen elimination was given by Mummery (*413*) in 1908. This paper is particularly useful in summarizing the work of Haldane and of Damant.

Findlay and Creighton (*399*) 1910–11 reported on the solubilities of various gases in water, ox blood, and ox serum under pressures ranging from 760 mm. Hg to 1,400 mm. Hg.

Conant and Scott (*396*) 1926 found that hemoglobin in contact with pure nitrogen takes up a little less nitrogen than it does from the air, but still much more than would be dissolved in water. The author suggested that carbon monoxide and oxygen are adsorbed by the blood.

The solubility of ethylene, acetelyne, and nitrogen in water and in blood were found to

follow Henry's law, according to Grollman (*403*) 1929. Blood lipoids were found to increase the solubility of these gases in aqueous solutions. According to Stoddard (*420*) 1927 the solubility of nitrogen in plasma protein solutions is influenced by the fat content.

Campbell and Hill (*393*) 1931 determined the nitrogen content in the bone-marrow fat of the ox, horse, and sheep breathing air. This was found to be 5 cc. of nitrogen per 100 cc. of fat. In calf and guinea pig brain, the content of nitrogen was 1 cc. per 100 cc. of tissue. Both of these values were determined at 1 atmosphere. The brain of a guinea pig exposed to a pressure of 9 atmospheres for 30 minutes contained 4.3 cc. of nitrogen per 100 cc. of tissue. Campbell and Hill also determined the nitrogen content of the human body by rebreathing oxygen into bags. Two hundred to 300 cc. of nitrogen were exhaled in 8 to 10 minutes. This comprised all the easily removable nitrogen. This quantity was doubled or tripled by exposure for 40 minutes to a pressure of 2 or 3 atmospheres (absolute) respectively.

In further experiments, Campbell and Hill (*394*) 1933 subjected goats to 4 atmospheres (absolute) breathing air. The animals were sacrificed while under pressure, the bones cut up and the marrow excised and placed immediately under water. The gases were extracted and analyzed. Goat bone marrow varies in its nitrogen absorbing capacity because of a variation in fat content. In marrow containing 90 percent fat, the tissue was 25 percent saturated with nitrogen in 1 hour, 60 percent saturated in 4 hours and 90 percent saturated in 8 hours. Campbell (*392*) 1933 determined the gaseous nitrogen content of various fatty acids, etc., saturated with air. The solubility of nitrogen in formic acid was found to be the same as for organic acid, liquid paraffin, acetone, stearin, palmitin, olein, and bone marrow. The solubility of nitrogen in all fats tested was found to be approximately the same, namely, 5 cc. of nitrogen in 100 cc. of fat. According to Campbell and Hill (*395*) 1933, liver, brain, and bone marrow were only 50 percent saturated with nitrogen after 3 to 5 hours' exposure to 4 to 6 atmospheres (absolute) of air.

Van Slyke, Dillon, and Margaria (*423*) 1934 determined the solubility and physical state of atmospheric nitrogen in blood cells and plasma. The solubility of nitrogen in whole blood was found to increase with a rise in the hemoglobin content and the solubility of nitrogen in plasma was found to be 8 percent less than that in water. The authors found no evidence of adsorption onto solids. The coefficients of solubility of nitrogen were determined as follows: in water, 0.01272; in plasma, 0.0117; and in cells, 0.0146.

In studies on the equilibrium time of the gaseous nitrogen in the dog's body following changes of nitrogen tension in the lungs, Shaw, Behnke, Messer, Thomson, and Motley (*417*) 1935 found that the total nitrogen varied with the total amount of fat in the body. Anesthetized dogs were desaturated of nitrogen by breathing oxygen and the time for total desaturation determined. Desaturated animals were then exposed to air at different pressures up to 4 atmospheres, and saturation times determined as well as rates of desaturation after complete or partial saturation at various pressures. The authors found that the rate of saturation is proportional to the partial pressure of the nitrogen breathed. The rate of saturation is equal to the rate of desaturation.

Behnke, Thomson, and Shaw (*385*) 1935–36 studied the rate of nitrogen elimination in three healthy human subjects. At normal atmospheric pressure, the nitrogen content of a 60 kg. man was 840 cc. Ninety-eight percent of this was eliminated during 6 hours of breathing oxygen. Nitrogen elimination follows an exponential curve, the slope of which is a function of the cardiac output. The rate of absorption and time of elimination can be estimated on the basis of the curve and the ratio of the solubility of the gas in fat to its solubility in water. Divers who have been exposed to pressure only a short time, say 20 minutes, can be decompressed rapidly because the unsaturated body fats and lipoids act as buffers against bubble formation.

Application of measurements of nitrogen elimination to the problem of decompressing divers was discussed in 1937 by Behnke (*384*).

Behnke and Willmon (*386*) 1940–41 carried out tests on 11 divers to determine gaseous nitrogen and helium elimination from the body during rest and exercise. The subjects breathed mixtures containing 73 to 76 percent helium, 5 to 7 percent nitrogen and 19 to 20 percent oxygen for 3½ hours and the results were compared with breathing air. It was found that the tissues of the body absorbed approximately 40 percent as much helium as nitrogen and that helium was eliminated in one-half the time required for nitrogen elimination. Exercise hastens gas elimination, mostly during the first 30 minutes. Gas elimination was found to be rapid from the fluids of the body and slow from the bone marrow. Nine to twelve hours were required for complete elimination of nitrogen after saturation.

Cutaneous diffusion of helium in relation to peripheral blood flow and the absorption of atmospheric nitrogen through the skin were considered by Behnke and Willmon (*387*) 1940–41. At 27° to 28° C. it was found that 40 to 60 cc. of helium diffused through the skin per hour while at 35° C. 170 cc. of helium diffused through the skin per hour. The amount of nitrogen or helium absorbed was determined by the amount in the exhaled air. The rate of diffusion of nitrogen was roughly one-half that of helium. Willmon and Behnke (*429*) 1940–41 subjected divers to a pressure of 44.5 lb. per sq. in. in a pressure chamber for 60 to 75 minutes. It was found on stage decompression that nitrogen was eliminated more rapidly when oxygen was breathed at a simulated depth of 50 to 60 ft. than at higher or lower simulated levels. At a simulated depth of 100 ft., the elimination of nitrogen was slow due to vasoconstriction and slowed circulation. A sharp increase was found in the amount of oxygen absorbed at simulated depths greater than 70 ft. because of the solution of oxygen in the tissues as a result of high pressure.

Shilling, Hawkins, Polak, and Hansen (*418*) 1935 carried out an analysis of 2,143 dives in the Experimental Diving Unit, Navy Yard, Washington, D. C. at simulated depths up to 200 ft. to discover the relationship of depth of dive, duration of pressure, and time of decompression with the occurrence of caisson disease. A definite correlation was found between the incidence of caisson disease and the theoretical saturation of tissues with nitrogen. Hawkins and Shilling (*404*) 1936 found that the solubility of nitrogen in ox or dog blood and water follows Henry's law, varying directly with the pressure of the gas. The solubility coefficient of nitrogen in water was found to be 0.0125 to 0.0132 (cc. of nitrogen per cc. of water). For blood it is 0.0135 to 0.0148.

In 1942, Scholander and Edwards (*416*) reported that 80 to 90 percent of the nitrogen in the blood and saliva was cleared within the first 10 minutes of oxygen breathing. The remaining 10 to 20 percent was lost gradually within the next 50 minutes. On breathing air again, the nitrogen content showed a transient rise above normal.

According to McArdle (*411*) 1945, the value of breathing pure oxygen to prevent the "bends" depends upon the rate at which nitrogen is eliminated by this process. McArdle determined the dissolved nitrogen of the cerebrospinal fluid of young and middle-aged subjects by the method of Van Slyke, Dillon, and Margaria (*423*) 1934. Eight subjects inhaled pure oxygen for varying periods. It was found that the rate of elimination of nitrogen follows a curve in which elimination would be complete in about 6 hours. Comparison of McArdle's cerebrospinal fluid nitrogen elimination curve with the nitrogen elimination curve determined by Behnke for water and fat indicates that the nitrogen in the cerebrospinal fluid is relatively slowly eliminated though not as slowly as from the fat of the body. This was assumed to be due to the relatively small area in which the cerebrospinal fluid is in contact with vascular structures.

For reports on the solubility of helium, reference may be made to papers by Ramsay, Collie, and Travers (*415*) 1895; Estreicher (*397*) 1899; Cady, Elsey, and Berger (*391*) 1922; and Hawkins and Shilling (*405*) 1936. For other reports relating to nitrogen saturation and elimination, papers by the following authors may be consulted: Fanjung (*398*) 1894; Fox (*400*) 1909; Bornstein (*390*) 1914;

Ubbelohde and Svanoe (*422*) 1919; Peters (*414*) 1923; Van Slyke, Wu, and McLean (*426*) 1923; Van Slyke and Sendroy (*425*) 1928; Van Slyke, Sendroy, Hastings, and Neill (*424*) 1928; Lee, Phelps, and Wilson (*410*) 1941; Wilson and Wilson (*431*) 1941; and Wilson, Lee, and Wilson (*430*) 1942.

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D. FAT CONTENT OF THE BODY

Since nitrogen is considerably more soluble in fat than in blood or other aqueous solutions in the body, it becomes important to determine the fat content of the human body with some accuracy. In 1829, Davy (*436*) reported studies of the specific gravity of different parts of the human body. Boycott and Damant (*434*) 1908 conducted experiments on rats, guinea pigs, and doormice and found that fatty animals had a higher fatality and illness rate following a rapid decompression than thinner animals. According to Boycott and Damant (*435*) 1908, the total fat content of female guinea pigs, rats, and mice was relatively greater than in males. In general, the fat content increased with age. For further studies on the fat content of the body, reference may be made to papers by Noyons and Jongbloed (*437*) 1934-35 and Behnke (*433, 432*) 1942 and 1944.

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E. OXYGEN AND CARBON DIOXIDE TISSUE TENSION

Campbell (*439*) 1925 injected air subcutaneously and intraperitoneally in an unanesthetized rabbit and examined the effect of breathing various percentages of oxygen. On breathing 90.77 percent oxygen at atmospheric pressure, there was an increase in the oxygen tension and carbon dioxide tension both under the skin and in the abdominal cavity. On breathing 11 percent oxygen, the oxygen and carbon dioxide tensions in skin and abdominal cavity fell. Campbell (*438*) 1922–23 also investigated the carbon dioxide partial pressure in various body cavities and tissue spaces under different conditions.

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III. PHYSIOLOGICAL EFFECTS OF LOW OXYGEN AND HIGH CARBON DIOXIDE CONTENT OF ENVIRONMENTAL AIR.

A. GENERAL STUDIES

As personnel rebreathe the air in a submerged submarine or any other closed compartment, the oxygen concentration will fall, whereas the carbon dioxide concentration will show a corresponding steady rise. Experiments have shown that these changes both in carbon dioxide and oxygen concentration follow a straightline course at least in experiments lasting up to 60 hours. Within closed compartments the times of survival of enclosed personnel will depend upon the following factors: (a) the total volume of air within the confined space; (b) the total number of personnel; (c) the rate of oxygen consumption and carbon dioxide output per man per hour. (This will depend upon the size of the men concerned and activity and emotional stress of such personnel. As the carbon dioxide concentration rises to levels of 3 to 5 percent, the oxygen consumption may tend to increase as a result of increased ventilation and accelerated metabolic activity in response to the excitant action of carbon dioxide. With concentrations of carbon dioxide around 7 and 8 percent, the bodily reactions will probably reach their maximum intensity. At about 10 percent, there occurs a breaking point and a rapid falling off of oxygen consumption as the homeostatic mechanisms of the body begin abruptly to fall.) (d) Times of survival will depend also upon individual tolerance of personnel to reduced oxygen and raised carbon dioxide concentrations. This individual tolerance may show wide variations from one man to another. As a survey of the literature that follows will show, species differences in carbon dioxide tolerance also exist, many animals being much more resistant to carbon dioxide concentrations than human beings. (e) Other factors affecting survival may be temperature, humidity, and the concentrations of carbon monoxide produced by imperfect combustion of various fuels, etc.

In the submarine, the atmospheric pressure remains essentially at sea-level pressure. In the diver's helmet, however, excess concentrations of carbon dioxide are present under

greatly increased pressures and since the effect of carbon dioxide on the body depends upon the total partial pressure of the gas, the action of a given percentage of carbon dioxide will be potentiated by high atmospheric pressures. The concentration of carbon dioxide and of oxygen in caissons and the working chambers of tunneling operations must also be a matter of concern. Ventilation of such chambers is extremely important. In the references which follow, the literature on the effects of low oxygen concentrations, as well as raised carbon dioxide concentrations, has been included. In some reports, the effects of low oxygen and high carbon dioxide in the same environment are considered, while in other papers the effects of these two factors have been investigated separately.

The literature on the effects of anoxia, quoted here, is purposely not complete. For a comprehensive collection of the published papers on this subject, reference should be made to Hoff and Fulton (*3*) 1942 and Hoff, Hoff, and Fulton (*4*) 1944. In regard to the published literature on the physiological and pathological effects of raised carbon dioxide tensions, only those references have been selected which were believed to be useful to medical officers and research workers in submarine and compressed air medicine. The reader will note a number of references included here which do not bear directly upon the practical problems presented by actual submarine environments; however, it is hoped that the reports that have been gathered together will provide a satisfactory background for an understanding of the basic physiology involved. Most of these papers on the physiological action of low oxygen and high carbon dioxide concentrations have been included without comment.

There is extensive literature on the toxic effects of high concentrations of carbon dioxide on human subjects and experimental animals. As early as 1875, Guichard (*461*) observed the deleterious effects of carbon dioxide under pressure and in 1878–79, Friedländer and Herter (*460*) conducted extensive experiments on the action of high percentages of carbon dioxide and low oxygen concentrations on rabbits. A rabbit placed in a gas mixture containing 12.9 percent carbon dioxide and 17.5 percent oxygen showed no narcotic effects after 1 hour and 35 minutes, at which time the carbon dioxide had risen to 13.3 percent and the oxygen concentration had fallen to 14.5 percent. On increasing the carbon dioxide concentration to 25 to 30 percent, the animal was rendered unconscious in a few minutes. From these and a number of similar experiments carried out on rabbits, it was concluded by Friedländer and Herter that concentrations of carbon dioxide of about 20 percent exert no really poisonous action upon rabbits during an hour's period. There is, however, an increase of respiratory activity and an increase in the work of the heart. With concentrations of carbon dioxide of 30 percent or over, rabbits show some depressant effect. The respiration is slower and weaker and the blood pressure gradually falls. Voluntary and reflex movements become weaker and then cease. The temperature falls slowly. These changes were observed to take place gradually over several hours. With maximal carbon dioxide concentrations (approximately 60 to 70 percent), depression occurred very early and, within a few minutes, voluntary and reflex motions ceased. Death occurred from embarrassment of respiratory and cardiac activity often within one-half hour. Obviously the rabbit shows a tolerance to carbon dioxide which is much greater than the resistance of human subjects.

Bert carried out several studies on asphyxia in confined spaces and on the effects of high concentrations of carbon dioxide, as well as studies on death from low oxygen concentrations in environments in which the carbon dioxide concentration was kept low by the use of carbon dioxide absorbents. Five of these papers (*448*, *449*, *450*, *451*, *452*) were published in 1873. Studies on the limits of respirable air were reported in 1891 by Étienne (*459*). This paper reviews Paul Bert's experiments on tolerance to low oxygen concentrations and Étienne estimated that the limit of life in a confined space is 6½ hours per man per cm. of space at 1 atmosphere.

Experiments on men in enclosed chambers

were also conducted by Haldane and Smith (*462*) 1892–93. These investigators noticed some hyperpnia when the carbon dioxide concentration reached approximately 2.5 percent. When the concentration reached 6.4 percent, the hyperpnia began to be unbearable. Nausea and frontal headache were also noted. If the carbon dioxide was absorbed by soda lime but the oxygen concentration gradually lowered by breathing a limited air supply, there was no nausea, hyperpnia, or headache even up to the time at which the subject lost consciousness from anoxia—at a level of 8.7 percent oxygen. Haldane and Smith determined that aqueous condensates of rebreathed air resulted in no ill effects when injected into rabbits, contrary to Brown-Sequard's theory of exhaled organic poisons. In 1913, studies of the effects of high carbon dioxide concentration and low oxygen concentration in submarines were conducted by Belli and Olivi (*447*). Observations were made of food intake, urinary and fecal output, body weight, and appetite. There was a fall in body weight but no change in dietary intake during a dive lasting 24 hours.

In 1930, Brown (*454*) published a detailed report on the effects of high carbon dioxide concentrations and the use of oxygen in preventing the ill effects of carbon dioxide. Tests were carried out in a 654 cu. ft. chamber on 11 human subjects and each experiment lasted from 5⅓ to 12 hours. Observations were made on the pulse and respiratory rate, minute volume of respiration, systolic and diastolic blood pressure, body temperature, and Schneider Index. In some experiments, a number of mental efficiency tests were conducted. In 3 experiments the final carbon dioxide concentration varied between 4.7 and 5.2 percent while the oxygen concentration ranged between 17.8 and 15.5 percent. Breathing 2 percent carbon dioxide caused no change in respiration except during exertion. The subjects were generally not conscious of increased respiratory effort until a concentration of approximately 3.5 percent carbon dioxide was reached. At the close of the tests, there was slight depression, headache, and a sense

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of chilliness and fatigue. The body temperature was subnormal and breathing labored but no actual sense of dyspnea was complained of at concentrations of carbon dioxide below 5 percent. With a carbon dioxide concentration of 5.2 percent and 15.8 percent oxygen, some shortness of breath was noticed at rest. Labored breathing became more rapidly progressive above 4.5 percent carbon dioxide than below. In 4 tests, the final carbon dioxide concentrations were 4.3 to 4.7 percent and the oxygen concentrations were 18.2 to 23.4 percent, oxygen being artificially supplied to the air mixture. In these experiments also, in spite of the added oxygen, there were subjective symptoms of depression, headache, chilliness, and fatigue. Depth and rate of breathing were not affected.

In a further group of three tests, the carbon dioxide reached concentrations of 5.6 to 5.8 percent while the oxygen level fell to 16.1 to 14.2 percent. The subjects were not conscious of increased effort of breathing at rest until approximately 3.5 percent carbon dioxide concentration was reached. In addition to depression, dyspnea, and headache, some subjects developed dizziness and nausea. The headache persisted for 1 to 3 hours after the tests. There was wide individual variation in the type and severity of symptoms. The body temperature fell 1° to 3° F. Presistent fatigue following the tests was an outstanding symptom.

A group of five tests were carried out in which oxygen was supplied and in which the final carbon dioxide concentrations reached 5.5 to 5.8 percent while the oxygen level varied between 18.5 and 21.9 percent. There was somewhat less dyspnea and fatigue than in the previous tests. Objective data showed but slight differences. Body temperature fell in both the low and high oxygen groups. With low oxygen concentrations and low carbon dioxide levels, initial symptoms of oxygen depression were noted at concentrations of 13 to 14 percent oxygen. If the carbon dioxide concentration was kept low, there was no sign of oxygen deficiency or other reaction at levels of 14 to 15 percent oxygen, whereas, at these latter oxygen levels with 5.8 percent carbon dioxide, there were severe symptoms.

The symptoms were lessened to some degree if the oxygen level was kept normal. With one exception, all subjects showed a rise in the Schneider-Index score at the higher carbon dioxide concentrations, the average increase in score being 4.3.

The Army Alpha, cancellation and addition tests, and tests of tensions and motor coordination, were conducted. There was some falling off in attention, memory association, and addition at a carbon dioxide concentration of 5.8 percent. However, the scores were not materially lowered for any of the types of measurement analyzed. Quite clearly, the subjects maintained an excellent psychological reserve under the conditions of the experiment. The author concluded that submarine personnel could carry on their usual duties for a protracted period if the carbon dioxide did not exceed 5 percent. Even at approximately 6 percent, men could probably still carry on for a short time. It was believed that the majority would be completely incapacitated at a level above 6 percent carbon dioxide. An adequate supply of oxygen tended to improve physical and mental efficiency at concentrations between 5 to 6 percent carbon dioxide but did not improve it at higher levels.

In a further investigation, Brown (*455*) 1930 reported that 6 percent carbon dioxide could be tolerated by human subjects for only 22 minutes and that at a concentration of 10.4 percent, carbon dioxide could be sustained for only a fraction of a minute. The respiratory rate was increased at this latter concentration and the pulse rate was accelerated. Systolic and diastolic blood pressure were both stated to be increased with a rise in carbon dioxide concentrations. The minute expiration volume increased up to 10.4 percent carbon dioxide and then began to fall. Subjective symptoms such as dyspnea, dizziness, flushing, stupefaction, apprehension, and headache were noticed. There was a considerable individual variation in resistance to carbon dioxide.

Certain Japanese reports are of interest. Moteki (*466*) 1931 and Moteki and Ikemoto (*467*, *468*) 1932 and 1934 found that human subjects sealed in an airtight tank commenced to feel symptoms when the carbon dioxide concentration reached a level of 2.73 percent with the oxygen at 17.6 percent. Concentrations of 5 to 6 percent carbon dioxide were stated to be tolerated if the oxygen concentration was maintained at normal levels. These investigators considered that the upper limits of vitiation of the air consistent with "slight labor" were reached with carbon dioxide concentration at 6 percent and the oxygen concentration at 14.5 percent.

Barcroft and Margaria (*446*) 1932 found that dialized cats breathing an air mixture containing 60 to 65 percent carbon dioxide and 25 percent oxygen soon showed gasping respirations and ceased to breathe. These animals have a much higher tolerance to carbon dioxide than human subjects.

In 1939, Alexander, Duff, Haldane, Ives, and Kenton (*442*) conducted experiments on carbon dioxide tolerance in human subjects. These experiments were occasioned by the loss of the British submarine, *Thetis*, from which only 4 out of 103 men escaped. One subject remained in a closed chamber for 16 hours without food or water. The carbon dioxide concentration rose from an initial level of 2.5 percent up to 6.6 percent at the end of the experiment. After 10 hours, there was panting but no distress. Subjects were confused and had headaches on leaving the chamber but no nausea. When the subject was put on the Davis escape device, he immediately vomited. The experiment was repeated later on 5 men who remained in the chamber for 1 hour with the carbon dioxide level at 6.1 to 6.7 percent and the oxygen at 18.7 percent. On making an escape with the Davis "lung," one vomited and 3 others were very ill. Investigators concluded that donning of the "lung" after long exposure to carbon dioxide may cause nausea, making it necessary to remove the "lung." It was suggested that men breathe air or oxygen for 30 minutes before trying to make good an escape with apparatus where vomiting is fatal.

In experiments conducted on white rats, Barbour and Seevers (*443*) 1943, determined the maximum tolerated concentration of carbon dioxide to be 15 percent. However, if the concentration of the gas were increased

very gradually over several days, animals tolerated levels of approximately 23 percent. Likewise, a greater degree of depression was produced by sudden exposure to a given concentration of carbon dioxide than by prolonged exposure to the same concentration, indicating that the rat is capable of certain degrees of acclimatization to carbon dioxide. Following sudden exposure to 11 percent carbon dioxide, there was a temporary decrease in the total oxygen consumption. This reached a level of 15 to 25 percent below normal in 2 to 4 hours and then slowly returned to the normal range after 24 hours of continuous exposure. When a rat was placed in an atmosphere with a gradually increasing concentration of carbon dioxide, the oxygen consumption remained normal until the carbon dioxide level was greater than 10 percent.

Barbour and Seevers (*444*) 1943 found that high levels of carbon dioxide produced a reversible state of narcosis in animals resembling in some ways both hibernation and anesthesia. This state could be induced and maintained for many hours in the rat and the dog by sudden exposure at 5° C. to a concentration of carbon dioxide of 5 percent or greater. A concentration of carbon dioxide of 11 percent caused a rise in blood carbon dioxide reaching as high as 110 volumes percent. The plasma pH attained a level of 7.07. A similar state was produced in the rabbit by cold and 20 percent carbon dioxide. Repeated exposure in the rat rendered the animal partially or completely resistant to carbon dioxide narcosis. A similar state of depression was produced by low oxygen tension (10 percent) and it was therefore concluded that a sudden and marked increase in carbon dioxide tissue tension results in a definite decrease in total oxidative metabolism.

For a review of the danger of asphyxia and its prevention from the naval standpoint, reference may be made to a paper published in 1939 by McIntire (*465*). Regarding submarine atmospheres, McIntire quotes the prevailing opinion that within a closed working space, such as a submarine, the concentration of carbon dioxide should not exceed 3 percent and that the oxygen concentration should not fall below 17 percent.

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B. SPECIAL SENSES

Gellhorn and Spiesman (*477*) 1934–35 carried out audiometric tests on 6 men breathing a carbon dioxide-air mixture containing more than 3 percent carbon dioxide. Breathing such a mixture resulted in a distinct loss in hearing from which there was recovery within 15 minutes after return to ordinary air. Voluntary hyperpnea caused a similar loss of auditory acuity as did also breathing oxygen concentrations of 7.5 to 15.8 percent. The hearing loss was more persistent after oxygen want than after breathing excess carbon dioxide. According to Gellhorn and Spiesman (*479*) 1935, hearing loss lasting for several hours resulted from breathing a 10 percent oxygen mixture for 10 to 30 minutes. Respiration of 4 to 8 percent carbon dioxide concentrations gave rapidly reversible depressions of auditory acuity. Visual intensity discrimination was also decreased according to Gellhorn (*476*) 1936, by oxygen lack (8 to 10 percent oxygen), carbon dioxide increase (6 percent), and hyperpnea. McFarland and Forbes (*483*) 1939 reported loss of dark adaptation under conditions of low oxygen.

Probably little actual change in sensory function occurs in an enclosed atmosphere containing up to 3 percent carbon dioxide and as little as 17 percent oxygen. At levels as high as 5 percent carbon dioxide and above, there may still be no consistent, significant changes in visual fields, auditory threshold, and discrimination or performance of pencil and paper tests, computation tests, and number checking tests. However, the nervous system is affected, as is indicated by greater body unsteadiness and loss of coordination and muscle power. At 5 percent carbon dioxide and 13 percent oxygen, gross bodily movements may not be severely affected. It seems quite likely that submarine personnel would be able to carry out their duties in an atmosphere containing a concentration of carbon dioxide of 5 percent and an oxygen level of 12.5 percent although these concentrations provide an environment close to the limits of tolerance of most personnel. In fixing the limits of carbon dioxide and oxygen, it should be remembered that individual differences in tolerance to such conditions do exist. In the absence of selection methods which exclude individuals with low tolerance, the limits should be fixed with these individuals in mind.

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C. NERVOUS SYSTEM

Haldane (*498*) 1924 called attention to muscular spasms, cramps, and hallucinations in human subjects exposed to 6 to 7 percent carbon dioxide. Moreover, at concentrations from 5 to 7 percent carbon dioxide, there is a decrease in the nystagmic movements artificially produced in human subjects, according to Gellhorn and Spiesman (*495*) 1935. Gellhorn and Joslyn (*492*) 1937 have shown that breathing 6 to 7 percent carbon dioxide causes a prolongation of time required for addition and cancellation tests and also increases the number of mistakes. Similar slowing of mental processes was produced in man by oxygen want (7 to 9 percent oxygen) and also by hyperpnea. According to Case and Haldane (489) 1941, concentrations of 3 to 4 percent carbon dioxide at 1 atmosphere resulted in no mental disturbances and, in some subjects, concentrations of carbon dioxide as high as 6 percent could be borne.

However, 4 percent carbon dioxide compressed to 10 atmospheres (equivalent to 4 percent carbon dioxide) caused marked mental confusion and a decrease in mental dexterity. Subjects breathing 6.6 to 9.7 percent carbon dioxide at 10 atmospheres lost consciousness in 1 to 5 minutes. It was found that low temperatures did not enhance the deleterious effects of high pressure or of raised carbon dioxide concentration alone but did increase the effects of both of these acting together. The paper of Case and Haldane should be consulted for a good bibliography and for vivid subjective accounts of symptoms.

For an excellent review of the narcotic properties of carbon dioxide, reference should be made to a report by Seevers (*507*) 1944. According to this author, a 5 percent carbon dioxide mixture is disagreeable and probably no human subject will remain conscious for more than 15 minutes breathing a 10 percent carbon dioxide mixture. Probably 4 to 6 percent carbon dioxide may be tolerable for a short while, but, at a concentration of 8 to 10 percent, the limits are nearly reached. At 10 to 12 percent carbon dioxide, there is unconsciousness if exposure is prolonged for more than 10 minutes. Levels of 10 to 15 percent are tolerable for only 1 to 2 minutes and concentrations of 15 to 25 percent are irrespirable except for a few seconds. At such concentrations, human subjects suffer from laryngeal spasm, headache, whooping inspiration, intolerable dyspnea, gross mental

confusion, and psychosis. At concentrations of 25 percent and above, there is complete narcosis and convulsions, either during or after exposure. Up to 10 percent, carbon dioxide appears to act as a respiratory and cardiovascular stimulant, but, above this critical level, the depressant effects of the gas begin to appear. Exposures of 5 to 6 percent for long periods may, according to Seevers, cause mental depression, ataxia, dizziness, and fatigue. In animals, concentrations less than 10 percent do not result in detectable narcotic action. However, concentrations above 30 percent will induce narcosis in most animals. At levels of 40 percent or above, animals show pulmonary edema, hemorrhages from the mucous membranes, and death in a relatively short time. Herbivorous animals tolerate slightly higher percentages than other animals; for example, rabbits have been exposed to 80 percent carbon dioxide for 15 minutes. Hibernating animals have also been shown to be more resistant to carbon dioxide. In the author's experiments, rats were able to survive 10 percent carbon dioxide indefinitely and very few succumbed at 15 percent. No rats survived 25 percent carbon dioxide for more than 36 hours and 50 percent carbon dioxide was lethal within 6 hours. Detectable depression was produced by concentrations of 20 percent or above but deep narcosis occurred only at 30 percent or above. In rabbits and dogs, as in man, carbon dioxide narcosis was associated with convulsions. At levels of 20 to 25 percent carbon dioxide, there was loss of appetite, weight loss (as high as 50 percent), moderate tetany, and mild convulsions for 12 hours after removal from the chamber. The majority of animals survived. On exposure of rats to 11 percent oxygen for 17 days, there was retention of base in the blood. Oxygen consumption was reduced to 75 percent of the control values in animals exposed to 11 percent carbon dioxide in spite of increased muscular activity associated with hyperpnea. At levels of 15 and 20 percent carbon dioxide, the oxygen consumption was reduced to 80 and 71 percent of normal, respectively. Ten percent carbon dioxide exerted no effect on oxygen consumption in rats and after acclimatization to carbon dioxide, oxygen consumption rose to a normal level. At 50°C., sudden exposure to 5 percent carbon dioxide in the rat or the dog induced a reversible state of narcosis. After several hours of exposure, there was a fall in body temperature with loss of reflexes and bradycardia. Previous fasting or previous exposure to 10 percent oxygen for 3 weeks also rendered animals more susceptible to carbon dioxide narcosis. Administration of thyroid also increased resistance to narcosis. Evidently, the essential factor in resistance to carbon dioxide narcosis prolonged the duration of pentobarbital and in rabbits 20 percent carbon dioxide resulted in a 25 percent prolongation of the time of action of amytal administered intravenously.

For a study of the psychological effects of oxygen deprivation in human subjects, reference may be made to a long monograph by McFarland (*505*) 1932. McFarland found that simple sensory and motor responses were not seriously affected until the subject was near collapse from oxygen want; then the loss appeared to be fairly sudden. Oxygen want did not disturb or impair simple habitual responses until it had become very severe or had continued for at least 1 hour below 10.25 percent without previous acclimatization. Kinesthesis and visual function were first affected; audition later. Multiple choice reactions were impaired at oxygen levels at about 11.5 percent and there was deterioration of neuromuscular control as demonstrated by loss of performance in pursuitmeter and handwriting tests. When the oxygen fell as low as approximately 9 percent, there was loss of memory, as well as loss of awareness of lapse of time. The effects of low oxygen on higher mental processes depended to some extent upon the emotional tendencies of the subject. Some individuals became lethargic or indifferent while others experienced emotional outbursts, hysteria, anger, etc. Basic personality patterns tended to be unmasked.

Disorders of mental functioning produced by low oxygen tensions have also been investigated by Barach and Kagan (*487*) 1940. In this study, 17 medical students and 9

patients were exposed to 13 percent oxygen for 3 hours. The students complained of frontal headache, dizziness, yawning, oppressive pains in the joints and epigastrium, tingling in the fingers and toes, and a vague anxiety. There was some inability to concentrate and perception time was slower. Fifty-nine percent of the subjects showed periods of elation succeeded by dullness and drowsiness. In 40 percent, there was no elation, but there was irritability and impaired performance on the psychological tests. In the 9 patients (suffering from psychoneurosis) the somatic complaints were essentially the same as those in the students but less pronounced and less frequent. Fifty-three of the patients showed excitement, loss of inhibitions, overt sexual advances, exaggerated self-esteem, etc. The others were dull and drowsy. The students made 45.4 percent more errors in the "retention and recall" test after 13 percent oxygen while the patients showed 19.2 percent *less* errors as compared with their performance in normal air. The Rorschach test after low oxygen showed only superficial changes indicating a swing in mood: 11 out of the 17 students were in a state of elation, and 6 showed a tendency toward depression with reduced ability to form new and original associations. It appeared, therefore, that anoxia exposed and exaggerated the preexisting tendencies to react according to fundamental inherent patterns. The inhalation of high oxygen atmospheres by patients with previously existing chronic anoxia may also produce a profound disturbance in mental functioning, according to Barach and Kagan. Irritability, stupor, and delirium may supervene within 3 hours of exposure to 50 percent oxygen tension. However, when these patients, become acclimatized to raised oxygen tension, the mental disturbance disappears and is frequently replaced by a cheerful and optimistic mental state.

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E. HEART AND CIRCULATION

At carbon dioxide levels of 5 percent and 13 percent oxygen, there is a rise in pulse rate and systolic blood pressure, headache, pallor, sweating, dizziness, and occasionally nausea (in approximately 20 percent of personnel). Beyond 5 percent carbon dioxide, toxic effects become more and more profound as evidenced by increased stimulation of the cardiovascular system. The action of high carbon dioxide on the heart and vascular system has been reported by Jerusalem and Starling (*539*) 1910, Itami (*538*) 1912–13, Lutz and Schneider (*545*) 1919–20, and Dale and Evans (*523*) 1922. At concentrations of carbon dioxide up to 7 percent with decreasing oxygen concentration or with the oxygen maintained at 30 percent, Schneider and Truesdell (*551*) 1922-23, found in human subjects an increase in pulse rate, a rise in systolic and diastolic blood pressure, as well as an increase in capillary and venous pressures. The hand volume increased at carbon dioxide levels up to 3 percent and then showed a decrease. Shaw and Gerrard (*553*) in 1924 carried out two tests in submarines under conditions simulating dives. The first test lasted for 22¾ hours and the carbon dioxide level at the end of the trial was 0.94 percent while the oxygen level had fallen to 16.37 percent. No objective or subjective symptoms of oxygen want or carbon dioxide excess were found. The average systolic blood pressure fell from 128 mm. Hg to 122.6 mm. Hg. The average pulse rate dropped from 71 to 68. In the second test, no attempt was made to absorb the carbon dioxide in the air during the first 12 hours and, after this time, the carbon dioxide concentration had risen to 2.27 percent while the oxygen concentration had fallen to 18.72 percent. There were insignifi-

cant changes in systolic and diastolic blood pressure and pulse rate. From the twelfth to the twenty-third hour, the carbon dioxide was absorbed and the level at the end of the run was 1.09 percent. The average systolic and diastolic blood pressures, as well as pulse rate, remained approximately unchanged. There were some complaints of slight headache after 12 hours but no noticeable discomfort.

Further studies on the cardiovascular effects of high carbon dioxide concentrations have been reported by Gollwitzer-Meier (*529*) 1929, Hayasaka and Itakura (*533*) 1931-1932, Bayliss (*521*) 1900-1901, Bronk and Gesell (*522*) 1927, and Wolff and Lennox (*557*) 1930. For additional studies of the effects of anoxia on the heart, papers by Gremels and Starling (*531*) 1926, and Rothschild and Kissin (*549*) 1931-32 may be consulted.

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F. BLOOD

Regarding the effects of high concentrations of carbon dioxide on the blood, Haldane and Smith (*567*) 1897–98 reported that increase in carbon dioxide concentration up to 6 percent did not decrease the absorption of oxygen. Popper (*581*) 1929 found that in animals acutely poisoned with carbon dioxide, there was an increase in serum globulin and a decrease in serum albumin. Henriques and Klausen (*570*) 1932 detected no essential changes in total serum protein or in the albumin-globulin ratio under conditions of raised carbon dioxide concentration. In human subjects breathing 5.3 to 6.8 percent carbon dioxide, there was a rise in blood sugar and a fall in blood lactic acid with no essential changes in the hemoglobin concentration, according to Itakura and Hayasaka (*572*) 1932. Miller (*578*) 1940 exposed normal dogs to concentrations of carbon dioxide of 1.5 to 5.0 percent over a period of 1 to 4 weeks. At the end of this time, there was a mild acidosis, the pH changing from 7.38 to 7.26; there was also a decline in the carbon dioxide combining power and a shift of chloride from the plasma to the erythrocytes with a decrease in total blood chlorides. There was also an increase in the cell-plasma bicarbonate ratio as well as in erythrocyte volume. The red cell count and white cell count were increased and there was a 5.3 percent increase in hemoglobin value. No change in the differential white count was reported.

Effects of low oxygen upon the blood picture have been studied by a large number of investigators. Some of these studies are reported in references given below. For further literature on this subject, the reader should consult references given by Hoff and Fulton (*3*) 1942 and Hoff, Hoff, and Fulton (*4*) 1944.

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G. LYMPH AND CEREBROSPINAL FLUID

For studies on the effects of low oxygen and high carbon dioxide on the cerebrospinal fluid, reference may be made to reports by the following authors: Nicholson (*588, 589*) 1928–29 and 1931–32; Maurer (*587*) 1940-41; and White, Verlot, Selverstone, and Beecher (*590*) 1942.

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H. RESPIRATION

The effects of raised carbon dioxide concentration and diminished oxygen concentration on respiration have also been carefully studied. In 1789, Seguin and Lavoisier (*641*) reported an acceleration of respiration as a result of breathing high concentrations of carbon dioxide. Snow (*644*) 1846 placed animals in closed chambers and studied their tolerance to vitiated air. When the oxygen concentration was kept constant (21 percent) and the carbon dioxide concentration allowed to increase, it was found that at a level of 12 percent carbon dioxide, birds began to be asphyxiated in 2 hours. At 20 percent carbon dioxide, there were evidences of asphyxia in birds within a few minutes. A mouse was killed in a 20 percent carbon dioxide mixture in 1½ hours. In a mixture of 6 percent carbon dioxide and 19.75 percent oxygen, birds showed hyperpnea in 10 minutes and died in 4½ hours. At 10 percent carbon dioxide and 19 percent oxygen, mice were hypernic in 10 minutes but recovered after being removed from the chamber at the end of 3 hours. One and one-half percent carbon dioxide and 19 percent oxygen had no adverse effect on birds. Three percent carbon dioxide and 16.75 percent oxygen resulted in hyperpnea but if animals were withdrawn, they recovered.

Hill and Flack (*618*) 1908 reported that hyperpnea resulted in dogs from breathing 15 to 30 percent carbon dioxide, whereas, 30 to 35 percent carbon dioxide exerted a depressant, narcotic action. The respiratory center, as Haldane and Priestley (*612*) 1904-5 have shown, is extremely sensitive to increased alveolar carbon dioxide tension, a rise of 0.2 percent of an atmosphere being sufficient to double the lung ventilation. At rest, when the oxygen pressure in the inspired air falls below about 13 percent of 1 atmosphere, the respiratory center begins to be excited by oxygen want and the carbon dioxide alveolar pressure commences to fall. Regulation of alveolar ventilation under ordinary conditions depends exclusively on the carbon dioxide pressure in the respiratory center.

For further studies on the effects of raised carbon dioxide concentrations on respiration, reference may be made to reports by Schneider (*638*) 1922, Padget (*633*) 1927–28, Barcroft and Margaria (*591*) 1931, Gesell and Moyer (*606*) 1934–35, and Shock and Soley (*642*) 1940.

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I. ALIMENTARY TRACT

The effects of varying the concentration of carbon dioxide and oxygen in the inspired air upon salivary secretion have been reported by Eddy (*653*) 1929, and the action of raised carbon dioxide pressures on gastric secretion has been investigated by Lepel (*654*) 1944.

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J. METABOLISM

For studies on the metabolic effects of high concentrations of carbon dioxide, reference should be made to reports by the following authors: McGinty and Gesell (*663*) 1925-26, Laubender (*662*) 1932, Büttner (*655*) 1934, Kodera (*658*, *659*) 1934, Gellhorn (*657*) 1937, and Dienst (*656*) 1943.

655. Büttner, H. E. Das Verhalten des Reststickstoffes im Blut nach Gaben von Arsen, Phosphor, chlorsaurem Natrium und bei Sauerstoffmangel. *Z. ges. exp. Med.*, 1934, *93:* 391–401.

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663. McGinty, D. A. and R. Gesell. On the chemical regulation of respiration. II. A quantitative study of the accumulation of lactic acid in the isolated brain during anaerobic conditions and the rôle of lactic acid as a continuous regulator of respiration. *Amer. J. Physiol.*, 1925–26, *75:* 70–83.

K. RENAL FUNCTION

The action of oxygen-poor, carbon dioxide-rich air on renal function has been reported by Edie (*666*) 1906; David, Bache, and Auel (*665*) 1914; and Auel (*664*) 1913-14.

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L. SPLEEN

Antal and Schleinzer (*667*) 1941-42 have reported on the functions of the spleen in relation to raised carbon dioxide and low oxygen tensions.

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M. INFLAMMATION

The relation of 6 to 8 percent carbon dioxide on inflammatory processes has been reported by Laubender (*668*) 1932.

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N. NEOPLASM

669. Campbell, J. A. Influence of low oxygen pressure in the atmosphere upon incidence of primary lung tumours in mice. *Brit. med. J.*, 1940, *1:* 336–339.

IV. PHYSIOLOGICAL RESPONSES TO HEAT, COLD, AND HUMIDITY

A. TEMPERATURE AND HUMIDITY PROBLEMS IN SUBMARINES

Before the installation of air-conditioning equipment in submarines, high temperature and humidity constituted important limiting factors in efficient performance of combat duty. In the present section, the effects of extremes of temperature and humidity upon body function will be considered. While these effects are characteristic, it has now come to be recognized that physiological adjustments to such extreme environments are such that personnel may often carry out their duties without measurable loss of efficiency up to a point just preceding collapse. It is especially true that under the stress of actual combat when the crew is highly motivated, the quality of performance may show little or no deterioration for a considerable period in spite of grossly unfavorable conditions of temperature and humidity. For this reason, it may be difficult to present arguments in favor of installing air-conditioning apparatus, particularly as economy of space and weight is of utmost importance in submarines. The submarine is a weapon of aggressive warfare and its chief function is to deliver torpedoes to enemy targets in the most efficient manner possible. Only such equipment may be installed on board a submarine which will contribute to the carrying out of its military mission. Quite rightly, therefore, provisions which increase the habitability of the vessel from the human point of view must be judged in the light of over-all military efficiency. In the case of air conditioning, there can be no doubt whatever that this development has increased the range, performance, and efficiency of the submarine as a combat vessel. Although it may be difficult under laboratory conditions to demonstrate a significant difference in objective performance when the temperature and humidity are maintained at optimal levels, nevertheless, operational performance as a whole under actual conditions is improved. Routine tasks, particularly when cruising for prolonged periods on the surface or submerged,

appear to be carried out with greater efficiency. Under the stress of an acute combat emergency, personnel may rise above unfavorable environmental conditions. The body is capable of these "spurts". However in the routine duties, unfavorable environmental conditions begin to take their toll. Furthermore, the maintenance of comfort conditions of temperature and humidity must also constitute a significant factor in the maintenance of morale.

It should be mentioned also that submarine surgeons have found a decrease in certain skin conditions in crews of submarines with air conditioning. Heat rash, boils, etc., present a much less severe problem. The control of vermin is also simplified.

B. GENERAL CONSIDERATIONS OF TEMPERATURE AND HUMIDITY

A surprisingly large number of early studies of the influence of humid air and relatively high temperature on the animal economy have been reported. One of these, a thesis by Le Borgne (*672*) published in 1831 in Paris, has been included as an example.

In 1927, Sayers and Davenport (*673*) reviewed the literature on the physiological effects of abnormal temperature and humidity. The pulse rate was recognized as furnishing a reliable indication of comfort and discomfort under conditions of various temperatures. When the pulse is above 135, the first symptoms of discomfort were stated to arise and a rate of above 160 was said to be associated with severe and distressing discomfort. The literature extant at the time of Sayers and Davenport's review contained no direct statement as to air conditions or length of exposure required to raise the body temperature to the lethal point. The lowest body temperature compatible with life was said to be approximately 78° F. According to one observer cited by Sayers and Davenport, the minimum accident frequency in factory work in both men and women was found to be at temperatures between 65° and 69° F. Accidents increased at lower temperatures until at 50° to 54° F., it was 35 percent greater than at 65° to 69° F. At temperatures below 49° F., the frequency of accidents fell off slightly, due probably to slower working rates. At temperatures above 75° F., the accident rate was 39 percent higher than at 65 to 69° F.

The reader is advised to consult a report by Harrington and Davenport (*671*) 1941 in which the authors outlined the effects of heat and humidity with particular application of health and safety in mines. The problems involved sufficiently resemble those with which the submarine surgeon or physician to caisson workers is concerned that this review may be examined with profit. As previously stated, the pulse rate was believed to furnish the best indication of discomfort at high temperatures. However, other investigators have considered body temperature as the most reliable index of the degree of tolerance or acclimatization. Harrington and Davenport's review considers various cardiovascular changes occurring in extremes of temperature and humidity and also discusses water loss. It is stated that soaking of the skin of workers in hot places results in diminished resistance to skin infections. Boils are prevalent in some mines in which the temperature is around, or over, 93°F. dry bulb or over 75°F. wet bulb. Skin affections among workers in high temperatures have been attributed to a change from the normal acid reaction of the skin to an alkaline reaction.

Regarding the effect of heat upon mental functions, it is stated that a rise in body temperature of as little as 1°F., may affect the psychological processes. The critical wet bulb temperature at which man is likely to collapse is said to be 93°F. Work in still, almost saturated air was easy at 75°F. At 80°F., the physiological effort required was greater, while at 90°F., it was impossible to endure the usual rate of work for a full hour. Tests on 23,000 miners who had worked for 2 to 6 years in British collieries showed that men working at a dry bulb temperature of 70°F., lost 3 percent of the time through sickness; at temperatures between 70° to 79°F., the time lost was 4.5 percent while at temperatures over 80°F., the time lost was 5 percent. At wet bulb temperatures below 66°F., 3 percent time was lost; between 66°and 69° F.wet bulb, the time lost was 4.2 percent; and at wet bulb tempera-

tures above 70°F., it was 5 percent. Between effective temperatures of 40° to 75°F., the amount of work performed was stated to be virtually constant. Above 75°F., the output fell rapidly.

It was considered inadvisable to allow the effective temperature to exceed 80°F. in heavy industrial operations. It was stated that human subjects can do almost twice as much work at 70°F. as at 93°F. and excessively warm environments increased the liability to accidents. Of 18,000 British coal miners, those working at temperatures of 80°F. or over had 30 to 70 percent more accidents than those working below 70°F. The increase in the severity of the accidents was less marked than the increase in frequency.

For a convenient summary of the effects of temperature and humidity, the reader may consult an article by Baetjer (*670*) 1943.

670. Baetjer, A. M. The effects of temperature and humidity on industrial workers. Pp. 69-90 in: *The principles and practice of industrial medicine.* Edited by Fred. J. Wampler. Baltimore, The Williams & Wilkins Company, 1943, xiv, 579 pp. [R, M]

671. Harrington, D. and S. J. Davenport. Review of literature on conditioning air for advancement of health and safety in mines. Part II. Need for air conditioning indicated by physical quality of underground air. *Inform. Circ. U. S. Bur. Min.*, 1941, no. 7182: 1-104. [R]

672.* Le Borgne, Gabriel. *Considérations sur l'influence de l'air humide et froid sur l'économie animale.* Thèse, Paris, 1831, vi. 23 pp.

673. Sayers, R. R. and S. J. Davenport. Review of literature on the physiological effects of abnormal temperatures and humidities. *Publ. Hlth. Rep., Wash.*, 1927, no. 1150: 1–63. [R]

C. PHYSIOLOGICAL EFFECTS OF RAISED TEMPERATURE AND HUMIDITY

For an early study on the physiological effects of raised humidity, the reader may consult a paper by Ronvaux (*688*) published in 1866. A brief historical consideration of the influence of high air temperatures and humidity is also to be found in a report published in 1905 by Haldane (*678*). Further studies on pulse rate and body temperature changes in humid conditions were reported in 1907 by Reichenbach and Heymann (*687*).

In experiments on the physiological effects of high temperatures and humidities, Sayers and Harrington (*689*) 1923 reported that at rest in saturated air at 91.5°F., for 1 hour with no air movement, subjects showed a rise in body temperature, a moderate increase in pulse rate and profuse sweating with dizziness and weakness occurring afterwards. With air movement, there was slight or no increase in body temperature, a rise in pulse rate and some sweating with no after effects. In subjects at rest in saturated air at a temperature of 95°F. for 1 hour with no air movement, there was a rise in body temperature, a marked rise in the pulse rate, very profuse sweating, dizziness on movement and an increase in the depth and rate of respiration. With air moving at the rate of 250 and 600 linear feet per minute, subjects exposed to saturated air at 95°F. for 1 hour showed slight or no increase in body temperature, a minimal or no increase in pulse rate, profuse sweating, but no untoward symptoms. With subjects at rest in saturated air at 96°F., with air still or in movement, there were symptoms which were practically the same as those felt in still or moving saturated air respectively at 95°F. Subjects exposed at rest to saturated air at a temperature of 98°F. for 1 hour with air movement showed a rise in body temperature with a considerable increase in pulse rate. Sweating was profuse, the clothes being saturated. In fact, sweat could be poured from the shoes when taken off. Subjects were dizzy and all felt that very little work could be done at this temperature. In subjects at rest in saturated air at 100°F. with no air movement, there was a marked rise in body temperature reaching as high as 102.3°F. The pulse rates varied from 152 in some subjects to more than 175. Subjects sweated profusely and dizziness and weakness were early and characteristic symptoms. These persisted for about 1 hour after the test. All symptoms occurred in spite of air movement and no subject was able to tolerate the conditions for a full hour.

McConnell, Houghten, and Yagloglou (*682*) 1924 pointed out that air motion has a cooling effect if the air temperature is below that of the body, the pulse rate rising rapidly as the surrounding temperature reaches the region

of discomfort. However, no constant correlation between pulse rate and body temperature was found. The systolic blood pressure was stated to increase as the temperature rose whereas the diastolic pressure was said to fall. There was peripheral vasodilatation.

For work tests conducted in atmospheres of high temperature and various humidities in still and moving air, the reader should consult a report by McConnell and Yaglou (*684*) 1925. Water and sodium chloride loss, rise in blood sugar, increase in pulse rate, and increase in arm volume in human subjects on exposure to hot, humid environment were reported by Böttner (*675*) 1941.

According to Thauer and Wezler (*691*) 1942–43, the systolic blood pressure in human subjects falls as the temperature rises from 15° to 30°C. and then increases from 30°C. to 50°C., but does not reach the 15° level. The diastolic pressure was reported as falling as the temperature goes from 15° to 50°C. The pulse rate was stated to increase as the temperature increases. At 15°C., the minute volume decreases over a period of 4 hours; at 30°C., it increases for 2 hours and then falls; at 50°C., there is a steady increase for 4 hours. The peripheral circulatory resistance increases if the subject is kept at 15°C., whereas it decreases in subjects exposed to a temperature of 50°C. The oxygen consumption showed irregular variations. However, the values for the 15°C. level run much higher than those for 30° to 50°C. levels. One subject showed a fall in body temperature as the room temperature was lowered from 24° to 15°C. There was no change in body temperature when the room temperature rose from 24° to 50°C.

According to Ito (*680*) 1936, high atmospheric temperature resulted in a rise in pulse rate and blood pressure. Asmussen (*674*) 1941 found little difference in cardiac output in work and rest at 22°C. and 27.6° to 30.6°C. Circulatory failure was stated to be more likely under conditions of humid heat. Sugawara (*690*) 1936 reported indefinite changes in the red blood count and a fall in the white blood count under conditions of high temperature. There was an increase in the percentage of neutrophile leucocytes.

According to McConnell, Yaglou, and Fulton (*683*, *685*) 1924 and 1925, the carbon dioxide output and oxygen consumption increase with exposure to high and low temperatures. The zone of minimal metabolic rate was found to lie between 75° and 83°F. effective temperature. Metabolic rates were excessive when the environmental temperature exceeded body temperature.

674. **Asmussen, E.** The cardiac output in rest and work in humid heat. *Amer. J. Physiol.*, 1941, *131:* 54–59.

675. **Böttner, H.** Das Verhalten des Menschen in heisser Umgebung. *Klin. Wschr.*, 1941, *20:* 471–475.

676. **Danilov, N. V.** [Certain features of blood circulation in high temperature.] *Fisiol. Zh. S.S.S.R.*, 1941, *30:* 87–98.

677. **Fukui, N., T. Sugita, and H. Ito.** On the latent B-avitaminosis in the subjects to sea service during the extreme hot season. *Bull. nav. med. Ass. Japan*, 1936, *25*(8): (English text pagination), 45–46. (In Japanese with English summary.)

678. **Haldane, J. S.** The influence of high air temperatures. No. I. *J. Hyg., Camb.*, 1905, *5:* 494–513. [P]

679. **Herrington, L. P. and A. P. Gagge.** Temperature regulation. *Annu. Rev. Physiol.*, 1943, *5:* 295–320. [R]

680. **Ito, M.** Effects of some kinds of medicine on the workers in the high atmospheric temperature. *Bull. nav. med. Ass. Japan*, 1936, *25*(12): (English text pagination), 81–82. (In Japanese with English summary.)

681. **McConnell, W. J. and F. C. Houghten.** Some physiological reactions to high temperatures and humidities. *Trans. Amer. Soc. Heat. Vent. Engrs.*, 1923, *29:* 129–162. [P]

682. **McConnell, W. J., F. C. Houghten, and C. P. Yagloglou.** Air motion—high temperatures and various humidities—reaction on human beings. *Trans. Amer. Soc. Heat. Vent. Engrs.*, 1924, *30:* 167–192. [P]

683. **McConnell, W. J., C. P. Yagloglou, and W. B. Fulton.** Basal metabolism before and after exposure to high temperatures and various humidities. *Publ. Hlth. Rep., Wash.*, 1924, no. 977: 3075–3088. [P]

684. **McConnell, W. J. and C. P. Yaglou.** Work tests conducted in atmospheres of high temperatures and various humidities in still and moving air. *Trans. Amer. Soc. Heat. Vent. Engrs.*, 1925, *31:* 101–122. [P]

685. **McConnell, W. J., C. P. Yaglou, and W. B. Fulton.** Basal metabolism before and after exposure to high temperatures and various humidities. *Trans. Amer. Soc. Heat. Vent. Engrs.*, 1925, *31:* 123–133. [P]

686. **Pitts, G. C., R. E. Johnson, and F. C. Johnson.** Work in the heat as affected by intake of water salt and glucose. *Amer. J. Physiol.*, 1944 *142:* 253–259. Abstr. *Bull. War Med.*, 1945, *5:* 430. [P, M]

687. Reichenbach, H. and B. Heymann. Untersuchungen über die Wirkungen klimatischer Faktoren auf den Menschen. II. Mitteilung: Beeinflussung der Kōrperwärme durch Arbeit und Beschränkung der Wärmeabgabe. *Z. Hyg. InfektKr.*, 1907, *57:* 23–49.

688. Ronvaux, J. Essai sur l'hygrométrie au point de vue physiologique, hygiénique et médical. *Ann. Soc. méd.-chir. Liége*, 1866, *5:* 8–16; 49–64. [C]

689. Sayers, R. R. and D. Harrington. Physiological effect of high temperatures and humidities with and without air movement. *Rep. Invest.* U. S. Bur. Min., 1923, no. 2464: 1–7. [P]

690. Sugawara, S. Experimental study of the influence of muscular labour of hot atmosphere on blood. *Bull. nav. med. Ass. Japan*, 1936, *25*(10): (English text pagination), 66–67. (In Japanese with English summary.)

691. Thauer, R. and K. Wezler. Wärmeregulatorische Umstellungen des Organismus bei wechselnden Klimabedingungen (Temperatur, Feuchtigkeit, Windgeschwindigkeit). II. Mitteilung. Kreislauf und Gaswechsel des Menschen bei verschiedenen Aussentemperaturen. *Luftfahrtmed.*, 1942–43, *7:* 237–259.

D. TOLERANCE AND ACCLIMATIZATION TO HEAT AND HUMIDITY

Winslow (*699*) 1917 stated that a temperature of 20°C. permitted most efficient work whereas with temperatures of 24° and 30°C. there was a definite decrease in efficiency of performance. With a rise in humidity, there was also a decrease in work performance. According to Yaglou (*700*) 1927, the comfort zone for men at rest, stripped to the waist, lies between 66° and 82°F., effective temperature, the optimum being 72.5°F. At 50 percent relative humidity, the optimum temperature with indoor clothing was found to be 70°F. dry bulb. In subjects stripped to the waist, the optimum dry bulb temperature was 80°F.

Droese (*693*) 1942 exposed 14 subjects to work conditions at room temperature and at 39°C. He found that at room temperature, the efficiency was improved by administration of glucose alone or a combination of glucose and vitamin B_1. At high temperatures, only the combination of glucose plus vitamin B_1 had any beneficial effect. It thus appears that heat increases the need for vitamin B_1.

Henschel, Taylor, and Keys (*695*) 1943–44 studied muscular work performance in 24 normal young men subjected to dry heat. Comparisons were made between the performances in heat on two occasions of 2 days each, separated by 1 to 4 weeks of cold weather. Work pulse rates, rectal temperatures, and vasomotor stability tests indicated persistence of heat acclimatization during at least 3 weeks of cold weather.

Factors affecting tolerance to heat and humidity were investigated experimentally by Bean, Eichna, and Ashe (*692*) 1944. Thirteen young garrison troops, acclimatized to dry and moist heat, exercised by walking at 3 miles per hour around the laboratory carrying a 20 lb. pack for 4 hours. The energy output was 300 calories per hour. Water containing 0.1 percent salt was given when asked for. Data were taken at a dry bulb temperature of 93° to 121°F. and a wet bulb temperature of 96°F. The wet bulb temperature was found to be an important limiting factor in determining the ability of men to work in hot climates whereas the dry bulb temperature was of minor importance. Below a wet bulb temperature of 91°F., men worked easily; between 91° and 94°F. wet bulb, subjects worked, but with difficulty. If the wet bulb temperature was 94°F. or over, it was impossible to work for as long as an hour. Near the upper limits, there was profuse sweating (2.5 to 3.5 liters per hour); the heart rate rose to 150 to 180; the rectal temperature rose to 102° to 103.5°F.; the skin temperature was 101°F.; and there was vomiting, headache, nausea, cramps, vertigo, weakness, dyspnea, collapse, and syncope.

According to Mills (*697*) 1944, metabolic acclimatization begins late in the second week of exposure and is largely accomplished at the end of the third week.

692. Bean, W. B., L. W. Eichna, and W. F. Ashe. The upper limits of heat and humidity tolerated by acclimatized men working in hot environments. *Proc. cent. Soc. clin. Res.*, 1944, *17:* 11–12. [P]

693. Droese, W. Die Wirkung von Traubenzucker und Traubenzucker B_1-Kombinationen auf die Leistungsfähigkeit bei Hitzarbeit. *Arbeitsphysiologie*, 1942, *12:* 124–133.

694. Eichna, L. W., W. F. Ashe, W. B. Bean, and W. B. Shelley. The upper limits of environmental heat and humidity tolerated by acclimatized men working in hot environments. *J. industr. Hyg.*, 1945, *27:* 59–84. Abstr. *Bull. Hyg.*, 1945, *20:* 480–481. [P, M]

695. Henschel, A., H. L. Taylor, and A. Keys. The persistence of heat acclimatization in man. *Amer. J. Physiol.*, 1943–44, *140:* 321–325. [P]

696. McConnell, W. J. and C. P. Yaglou. Work tests conducted in atmospheres of low temperatures in still and moving air. *Trans. Amer. Soc. Heat. Vent. Engrs.*, 1926, *32:* 237–248. [P]

697. Mills, C. A. Metabolic acclimatization to tropical heat. *Proc. cent. Soc. clin. Res.*, 1944, *17:* 12–13. [P]

698. Schlegel, B. Experimentelle Untersuchungen zur Besserung der Hitzeverträglichkeit des Menschen. *Klin. Wschr.*, 1941, *20:* 506–510.

699. Winslow, C.-E. A. The effect of atmospheric conditions upon fatigue and efficiency. *Amer. J. publ. Hlth.* 1917, *7:* 827–834. [P]

700. Yaglou, C. P. The comfort zone for men at rest and stripped to the waist. *J. industr. Hyg.*, 1927, *9:* 251–263. [P]

E. EFFECT OF HEAT AND HUMIDITY ON SUSCEPTIBILITY TO DISEASE

Reference has already been made to the fact that submarine personnel and miners working under conditions of high temperature and high humidity are particularly vulnerable to skin affections. The effect of hot and humid air upon susceptibility to other diseases has been a subject which has attracted clinical interest but upon which there is, nevertheless, not sufficient authoritative information.

The reader may wish to consult an early paper by Marc (*705*) 1828 on the influence of humid air on health and disease, and a thesis by Carrette (*703*) published in Paris in 1839 on the same subject. This author stressed the value of dry, warm air in the therapy of pulmonary tuberculosis and scrofula and claimed that syphilis is aggravated by humid atmospheres. In 1850, Jackson (*704*) discussed the comparative influence of dry and moist hot air in the causation of disease and argued against the sprinkling of streets. His arguments were supported by medical and literary references to the ill effects of humid air and the beneficial action of dry air. Baetjer and Lange (*701*) 1928 compared the effect of a temperature of 69°F. and 45 percent humidity on the susceptibility of guinea pigs to infection with tubercle bacilli. There was apparently no difference in the resistance of these animals to the infection under the warmer conditions. The effect of extremes of temperatures and humidity on resistance to disease is intimately bound up with the subject of climatology. The reader is referred to certain papers listed under that section (page No. 339). However, the subject as a whole is outside the province of the present volume.

701. Baetjer, A. M. and L. B. Lange. The effect of high humidity and moderately high temperature on the susceptibility and resistance to tuberculosis in guinea pigs. *Amer. J. Hyg.*, 1928, *8:* 935–946.

702. Bergonzini, C. Sulla respirazione d'aria calda coll'apparecchio di Weigert. *Rass. Sci. med.*, 1889, *4:* 264–267.

703. Carrette, Isidore. *De l'influence sur l'économie animale d'un changement dans l'état hygrométrique de l'air.* Thèse (Méd.) Paris, Imprimerie et Fonderie de Rignoux, 1839, 22 pp. [C]

704. Jackson, S. Some hints on the comparative influence of dry and moist hot air in the causation of disease. *Med. Exam. Rec. med. Sci.*, 1850, *6:* 319–333.

705. Marc, Jules. *L'influence de l'air humide sur l'économie animale.* Thèse (Méd.) Paris, Imprimerie de Didot le jeune, 1828, 30 pp. [C, R]

F. HEAT DISEASE

Hall and Wakefield (*713*) 1927 in a study of experimental heat stroke, noted that in 1858 Claude Bernard killed birds and mammals by raising the body temperature 4° to 5°C. In Hall and Wakefield's experiments, dogs were subjected to raised temperatures and high humidity in an experimental chamber in which the air was kept in motion by a fan. The animals showed increased depth and decreased rate of respiration as well as thirst, convulsive seizures, and loss of sphincter control. The rectal temperature rose by 4° to 10°C. There was an increase in nonprotein nitrogen, urea, creatinine, sugar, chlorides, calcium, and lactic acid in the blood. Also, slight decreases were noted in the pH, total nitrogen, and total solids. The carbon dioxide combining power of blood was definitely decreased. Urine was suppressed in all cases. At autopsy, the left ventricle was contracted, the venules congested and the stomach dilated and full of fluid. In some animals, thyroid damage was found.

Writing on the action of temperature and humidity in industrial occupations, Koelsch

(*716*) 1927 stated that the body can stand temperatures as high as 100°C. for 5 to 10 minutes if the air is dry. A temperature of 24°C. with a humidity of 80 percent is, however, unbearable. Subjects exposed to such conditions complained of headache, weakness, and restlessness. It was stated that a temperature of 25°C. with a humidity of 85 percent with the air in motion is more endurable than a temperature of 20°C. and 60 percent relative humidity in still air.

In a long paper on heat cramps, Talbott (*721*) 1935 gave a historical review of the literature, pointing out that Edsell was the first to investigate the disease as a clinical entity. The condition is associated with a decrease in bases and chlorides in the blood and an increase in serum protein. The condition is often fatal although mortality statistics are not sufficiently complete. The disease appears to be caused primarily by high temperature, whereas, humidity appears to be of less importance. Bad hygiene, recent untreated attacks of cramps, inadequate food and recent alcoholic bouts predispose to heat cramps. Clinically, the condition is characterized by involuntary spasmodic contractions of voluntary muscles. There is severe pain and the face is flushed. The muscles of the abdominal wall may be involved and in severe cases, the patient may be mentally distracted by the pain. There may also be mild vertigo and headache. The pain is apparently of peripheral origin arising from conditions within the muscle and not in the central nervous system. On cessation of cramps, the pain subsides. Cramps may occur at any time of day or night, usually within 18 hours of stopping work. Workmen themselves believe that sweating ceases before cramps occur but many patients suffering from cramps were seen to be sweating. According to Talbott, there is an increase in the red blood count, an increase in inorganic phosphate, and a tendency to acidosis. There is an increase in the calcium concentration of the blood and the blood sugar values are increased, as is the nonprotein nitrogen. The white blood cell count is increased by 4,000 to 6,000. The urine volume is usually increased in severe cases and the pH falls. There is a rise in the excretion of creatinine, and albumin is often found in the urine on the second or third day of the attack. Regarding pathology, there are but few autopsies available. It is of interest that in 2 cases, contraction of the left ventricle was recorded but the significance of this finding is not apparent. Heat cramps are treated by rest and administration of morphine to control pain. Hot baths are favored by some and administration of saline solution has been found very satisfactory. The condition may be prevented by adequate fluid and salt intake, by sufficient rest and a balanced diet. The reader will find three case histories given in Talbott's article.

In 1938, Ferris, Blankenhorn, Robinson, and Cullen (*711*) published a study of heatstroke in which clinical and chemical observations were made on 44 cases. The mortality in this condition ranges from 10 to 80 percent. The rectal temperature may rise to as high as 104° to 112°F. There is sudden collapse, weakness, and headache and the patient has a feeling of excessive heat. Prior to collapse, sweating ceases. The skin is hot and dry and the muscles are flaccid. There may also be a maculopapular skin rash. Some mental confusion may be encountered in conscious patients and the respiration is deep and sighing. Shock is seen only in extreme cases. There is some evidence of blood concentration, but the sodium and chloride levels are normal. The carbon dioxide content of the blood is low but not sufficiently to be responsible for coma.

Further studies on heat disease have been reported by Weiner (*723*) 1938, and Elias (*709*) 1942. Marshall (*717*) 1942 reported on the use of salt in troops exposed to heat. According to this author, increased consumption of salt in physical exertion at high temperatures results in greater efficiency and less fatigue, and prevents heat cramps and heat exhaustion.

Heat effects are also discussed in an article published in 1943 by Carleton and Kammer (*708*) and a brief report on the use of salt in tropical weather was published in 1943 by Flattery (*712*). Various pathological effects of

heat were reviewed in 1944 by Heilman (*714*), while Morton (*718*) reported on heat effects in British service personnel in Iraq in 1944.

706. Ancona, V. Dell'aria atmosferica ed in ispecie del vapor acqueo in rapporto colle angine e congiuntiviti catarrali. *Gazz. med. ital. Prov. Venete*, 1879, *22:* 67–72.

707. Bert, [ ]. Expériences relatives à la mort des animaux inférieurs par la chaleur. *Gaz. méd. Paris*, 1873, Sér. 4, *28:* 478. [C, P]

708. Carleton, E. H. and A. G. Kammer. Heat sickness. *Rocky Mtn med. J.*, 1943, *40:* 384–389.

709. Elias, F. J. Prevention and treatment of heat collapse among industrial workers. *Minn. Med.*, 1942, *25:* 972–973.

710. Fantus, B. The therapy of the cook county hospital. *J. Amer. med. Ass.*, 1934, *103:* 990–991.

711. Ferris, E. B., Jr., M. A. Blankenhorn, H. W. Robinson, and G. E. Cullen. Heat stroke: clinical and chemical observations on 44 cases. *J. clin. Invest.*, 1938, *17:* 249–262. [P]

712. Flattery, J. M. Experiences of salt deficiency. *Med. J. Aust.*, 1943, *1:* 5–7.

713. Hall, W. W. and E. G. Wakefield. A study of experimental heat-stroke. *J. Amer. med. Ass.*, 1927, *89:* 177–182.

714. Heilman, M. W. Heat disease. A clinical and laboratory study. Pp. 156–169 in: *Introduction to Industrial Medicine*. Edited by T. Lyle Hazlett. Pittsburgh, University of Pittsburgh, 1944, 216 pp. [R]

715. Heilman, M. W. and E. S. Montgomery. Heat disease: a clinical and laboratory study. *J. industr. Hyg.*, 1936, *18:* 651–667.

716. Koelsch, [ ]. Temperatur- und Feuchtigkeitswirkungen in gewerblichen Betrieben. *Arbeiterschutz*, 1927, No. 3, pp. 41–44.

717. Marshall, G. C. The use of salt in the prevention of heat fatigue and exhaustion. *Army med. Bull.*, 1942, No. 60, 114–115.

718. Morton, T. C. Heat effects in British service personnel in Iraq. *Trans. R. Soc. trop. Med. Hyg.*, 1944, *37:* 347–372. [P]

719. Skinner, J. B. and W. M. Fierce. The control of excessive heat and humidity in industry. *J. industr. Hyg.*, 1945, *27:* 31–35. Abstr. *Bull. Hyg.*, 1945, *20:* 481. [P, M]

720.* Smith, A. R. Heat relief. *Industr. Hyg. Bull.*, 1943, *22:* 253.

721. Talbott, J. H. Heat cramps. *Medicine, Baltimore*, 1935, *14:* 323–376. [R]

722. Wallace, A. W. Heat exhaustion. *Milit. Surg.*, 1943, *93:* 140–146.

723. Weiner, J. S. An experimental study of heat collapse. *J. industr. Hyg.*, 1938, *20:* 389–400. [P]

724. Wolkin, J., J. I. Goodman, and W. E. Kelley. Failure of the sweat mechanism in the desert. Thermogenic anhidrosis. *J. Amer. med. Ass.*, 1944, *124:* 478–482.

G. EFFECTS OF COLD

Knowledge of the effects of exposure to cold, particularly immersion in cold water, has been greatly extended during World War II. Most readers will be familiar through articles in the public press with experiments conducted on prisoners and internees in German concentration camps on the effects of exposure to cold and upon the value of rapid warming in such victims. The results of such research cannot easily be judged since the scientific honesty and integrity of many of the workers concerned is open to serious question.

Certain physiological effects of cold have been reported in the published literature and the reader may consult a paper by Yaglou (*732*) 1937 and a study published by Fröhlich (*725*) 1938–39. In the latter report, rabbits were immersed in iced water at a temperature of 1°C. for 8 to 15 minutes. The body temperature fell 7° to 14°C. The total leucocyte count was decreased in two cases and increased in one. The percentages of eosinophile and polymorphonuclear leucocytes were increased. There was a high percentage of injured and distorted leucocytes. According to Grow (*726*) 1940, patients suffering from chilling and frostbite may show warped judgement and distortion of intellect apparently the result of anoxia. Experiments with goats showed a fall in arterial oxygen saturation when the animals were chilled. In human subjects, there was a reduction in the arterio-venous oxygen difference. However, the author questioned whether exposure to cold reduced the capacity of the tissue to utilize oxygen. Oxygen administration was suggested in severe chilling as a therapeutic measure to obviate the psychological disturbances. von Werz (*731*) 1943 also considered oxygen lack to be responsible for death from exposure to cold.

Three papers published by Lewis (*727, 728, 729*) in 1941 on the injurious effects of cold upon the skin and underlying tissue are of importance. Entering cool or cold rooms causes a fall in the temperature of the exposed skin.

There is contraction of the cutaneous blood vessels of the body surface exposed to cold, and following this, transient reflex vasoconstriction in other parts of the body. Cooled blood from the peripheral circulation cools the general circulation, resulting in a lasting vasoconstriction. After 5 to 20 minutes, the cooled skin areas show a brief vasodilatation followed by vasoconstriction. The vasodilatation is stated by Lewis to be due to an axone response. It is accompanied by other reactions such as pitting, pain, tenderness, and local redness. Prolonged exposure to cold leads to swelling and pitting of the skin. The response is stated by Lewis to be similar to the reaction of histamine injection. Chilblains result from exposure to cold but not frost or freezing. Usually, prolonged exposure is necessary. The hands, legs, and other unprotected areas usually being effected. Frostbite has an effect on tissue similar to heat. It is characterized by local redness, wheal formation, flare, blistering, cellular exudate, vascular thrombi, and necrosis. The freezing may either be limited to the surface or may involve deep tissues. It is never encountered at temperatures above minus 2°C. and occurs only in dry air. Rubbing the frozen member is contraindicated as it is believed that this leads to necrosis of the damaged tissue. Gentle warming and slow thawing are recommended.

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H. RELATION OF CLOTHING TO THE EFFECTS OF TEMPERATURE AND HUMIDITY

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734. Nelbach, J. H. and L. P. Herrington. A note on the hygroscopic properties of clothing in relation to human heat loss. *Science*, 1942, *95:* 387–388. [P, M]

V. VISUAL PROBLEMS

United States submarine medical activities have played a significant part in research on vision. Reports on this work as well as other literature on the military aspects of vision have been compiled by Fulton, Hoff, and Perkins (*2*) 1945; Hoff and Fulton (*3*) 1942; and Hoff, Hoff, and Fulton (*4*) 1944. These bibliographies should be consulted for comprehensive lists. The references given below have been selected as being especially applicable to compressed air, diving, and submarine medicine. Reference may be made to submarine lighting on page No. 341.

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VI. ANATOMICAL AND PHYSIOLOGICAL ADAPTATIONS OF SUBMARINE ORGANISMS

Many species of animals, mammals, birds, and fish are adapted to a form of aquatic life which entails dives to considerable depths, often for prolonged periods. The adaptations which permit aquatic animals to hold their breath during submergence are of interest to the specialist in underwater medicine, particularly in relation to the deep dives undertaken by naked divers. It has also been a matter of some speculation that the whale which is capable of quite prolonged periods of submergence apparently does not suffer from decompression sickness. Since research on the adaptations of aquatic animals may, therefore, throw further light upon human problems in diving, certain pertinent literature on this subject is included here.

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A. DIVING MAMMALS

In 1939, Irving (*833*) published a review on the respiration of diving mammals. He pointed out that inhalation of oxygen in human subjects doubles the capacity to maintain voluntary apnea. Sponge divers can dive for about 2 minutes and various land mammals can hold their breath for approximately 1 minute. Diving animals are able to submerge for about 10 times as long. Whales may apparently remain submerged as long as 1 hour. Muskrats are capable of voluntary apnea for 12 minutes and beavers for 15 minutes. In many cases, the blood of diving animals has a greater than usual oxygen capacity; for example, the seal. This appears to be due to an increased concentration of red cells in addition to a greater oxygen capacity of the red blood corpuscles themselves. The heart rate of diving animals is retarded during the apnea of diving and the muscles become relaxed. Even out of water, a duck will hold its breath when the head and neck are extended. Excitation of proprioceptive sense organs in the neck apparently initiates the apnea mechanism in ducks during diving. In diving animals, control of the circulation reduces the flow of blood through muscles and increases the flow through the brain. Slowing of the heart and suppression of superfluous muscular activity add to the effectiveness of the adjustments made by the body. The physiological adjustments of diving animals differ only quantitatively from those of land mammals. No new mechanism is brought into play.

Irving discussed the question of the immunity of the whale to decompression sickness. The reason for this immunity is not yet clear and it may be that whales do suffer from the effects of rapid decompression under certain conditions. The physiology and biology of the whale is unfortunately not sufficiently well known and much of the information on the subject is unreliable. For example, we do not yet know all we should about the diving habits of the whale or the mechanisms of the respiratory exchange before and after diving. Beale

(*822*) 1839 in a monograph on the natural history of the sperm whale stated that this animal when surfaced makes one inspiration and one expiration every 10 seconds. The expiration (spout) lasts about 3 seconds and the inspiration about 1 second. A whale at the surface apparently makes about 60 to 70 expirations, remaining at the surface for 10 to 11 minutes. When he has had sufficient breathing time (or has had his "spoutings out," as it is called), he dives. According to Beale, the sperm whale may remain below surface for as long as 1 hour and 10 minutes. Some females were observed to remain below surface for approximately 20 minutes, with periods at the surface of 4 minutes (35 to 40 expirations).

According to Jolyet (*840*) 1893, the whale may take approximately three breaths per minute. These observations of Beale and of Jolyet are somewhat unreliable. A more authoritative report is that published by Allen (*821*) in 1916 on the whalebone whales of New England. This report contains a useful bibliography on whales up to 1914 and should be consulted by readers who are interested in the physiological adaptation of whales. The blue whale, like other large whales, carries out two types of diving: (a) a series of shallow or surface dives, and (b) deep dives in which the whale "sounds" or goes down for a long period. After coming to the surface from a deep dive, the blue whale makes about 12 to 15 shallow dives and then goes down again for a period of 5 to 10 minutes or more. At each short dive, the vertex of the head appears first and simultaneously the spout is delivered. The open nostrils then take in a breath and close with the sinking of the head which passes forward beneath the surface. The whale again comes to the surface, "blows" and then goes down again. When it has sufficiently refreshed its lungs by these shallow dives and "blows," the whale plunges into the depths. These shallow dives each last about 12 to 15 seconds.

Further data on the depths to which whales descend were provided in 1927 by Gray (*826*) who reported that large Greenland whales descend to a depth of 700 and 800 fathoms and may remain for nearly an hour when harpooned. It is questionable whether the behavior of whales when wounded gives any reliable indication of their normal diving habits and it is quite possible that when whales have submerged to great depths, after harpooning, they may suffer from manifestations of decompression sickness. As far as is known, however, gas bubbles have not been found in the blood or tissues of whales that have been caught.

How the whale avoids decompression sickness is still a matter of speculation. It has been suggested that the retia mirabilia may play a role. Ommanney (*845*) 1932 described the retia mirabilia in two fetuses of the fin whale which he dissected. The thoracic rete is a fatty, vascular mass lying at the anterior end of the thorax in the fork of the scalenus and the rectus capitis anticus major muscles. It is in contact with all vertebrae from the first and second cervical down to the fifth and sixth dorsal levels, and extends between their transverse processes up into the neural canal through the large foramina between the neural spines. Another vascular mass has been found lying against the basis cranii close to the tympanic bulla. Ommanney discussed the possible function of the retia mirabilia. He suggested that it may act as a kind of accessory lung, the fat absorbing oxygen from the blood during progression at the surface and returning it to the circulation during submergence. According to Ommanney, nitrogen may be similarly absorbed from the blood by the retia mirabilia as the whale ascends to the surface.

Laurie (*844*) 1933 carried out a very complete investigation of the physiological adaptations of whales. He estimated that the basal metabolic rate in blue whales and fin whales is approximately 2.25 calories per kg. of body weight per day. This compares with a rate in man of 32.9 calories per kg. per day, in the rabbit of 58.5 calories and in the guinea pig of 223.1 calories. It is thus seen that the basal metabolic rate of the whale is considerably lower than in smaller mammals. The weight of the lungs of the blue whale was found to be 1.2 percent of the soft parts, while the average weight of the human lungs is approximately 2.4 percent of the soft parts. On this basis, the

vital capacity of the whale may be estimated to be about one-half that of man in proportion to total weight. The total vital capacity of a whale weighing 1,226 kg. was estimated at 3,050 liters. These figures were based on the assumption that vital capacity is a function of the weight of the lungs. Laurie stated that whales probably remain submerged for 10 to 30 minutes, but he admitted that the data are not reliable as far as undisturbed whales are concerned. He quotes an observation by Scoresby in 1820 of a descent to 300 fathoms at a rate of about 8 to 10 miles per hour. This observation was made in a wounded whale who dived when struck by the harpoon and remained down for about 30 minutes. Wounded whales were reported to descend to 700 to 800 fathoms and according to Laurie, they ascend very exhausted. Laurie records that a blue whale dived straight down, taking with it 220 fathoms of line and remained below for 32 minutes. Racovitza is quoted as having estimated that whales not under special stimulus descend to a maximum of 100 m. Laurie, himself, reported the case of a sperm whale caught in a cable off the coast of Peru which had broken at 500 fathoms. Therefore, whales may sustain a pressure of 10 atmospheres under normal conditions and may tolerate even higher pressures under extreme provocation. Species differences in tolerance may exist.

Regarding the action of high pressure on the body of the whale, Laurie stated that pressure exerts its influence everywhere on the whale's body equally, internally as well as externally. The thorax does not act as a rigid wall protecting the heart and lungs from pressure.

Ommanney (*845*) believed that whales do not descend much deeper than 130 ft. He pointed out the danger of oxygen poisoning at greater depths. However, Laurie stated that there was a danger of oxygen poisoning only if there was an unlimited supply of oxygen to the lungs. The volume of oxygen taken down by the whale could be dissolved more than once over in the body fluids before the partial pressure of oxygen exceeded 1 atmosphere. In any case, according to Krogh (*842*) 1934, a large proportion of the oxygen in the lungs would be used up before the whale had reached any considerable depth.

Concerning the effects of carbon dioxide, Laurie recalled that the action of this gas depends not upon the percentage of carbon dioxide, but upon its partial pressure. A small percentage at a great depth will have an effect similar to a high percentage at a low pressure. The whale may be less sensitive to a wide range of blood carbon dioxide or possibly the respiratory center depends entirely upon oxygen lack for stimulation. Considerable volumes of carbon dioxide are found dissolved in the blood and in the body fluids of whales.

Contrary to popular belief, the whale is but little fatter than man. In the whale, the fat constitutes 20 to 24 percent of the total weight; while in normal men, the fat content is stated to be approximately 15 to 20 percent. Laurie carried out gas analysis of the urine, allantoic fluid, and blood. Large volumes of carbon dioxide were found in the urine and in the allantoic fluid, indicating that high partial pressures of this gas are common in the whale. A slight supersaturation of urine and allantoic fluid with nitrogen was also observed. Adult and fetal blood of whales was hardly ever found to contain as much dissolved nitrogen as the blood of other mammals at 1 atmosphere. The nitrogen capacity of the whale's blood was found to be more than twice that of human blood. Laurie reported that nitrogen tends to disappear in the blood and cannot be extracted from it by evacuation. This unique phenomenon appears to be contingent upon the presence of oxygen. It was not possible to measure the maximum rate of disappearance of nitrogen but the greatest volume of nitrogen removed was 2.7 volumes percent in 40 minutes. Laurie found small organisms approximately 0.5 μ to 2.0 μ in diameter in all samples of adult and fetal whale's blood. These organisms reproduced rapidly *in vitro* and were resistant to freezing. Crude cultures were capable of taking up more nitrogen gas than would be soluble in physical solution and of disposing of the nitrogen in some way so that it was not recoverable by evacuation. It was found that pig's blood when infected with these organisms behaved like whale's blood in

disposing of gaseous nitrogen. Laurie believed that these organisms are responsible for a kind of nitrogen fixation in whale's blood and that their presence in whale's blood serves to protect the whale from caisson disease.

Samples of whale's blood, when prepared in the form of wet smears, showed organisms to be approximately spherical. They were motile and there were about 10 to 30 million organisms per cu. mm. They were found to grow and reproduce not only in nutrient solutions (containing 1 percent glucose, 0.7 percent sodium chloride, and traces of sodium phosphate), but also upon plate cultures.

In commenting on Laurie's theory, Krogh (*842*) 1934 believed that a nitrogen fixing mechanism such as hypothesized by Laurie would not act rapidly enough. Also, he stated, nitrogen fixation requires oxygen not less probably than 1 volume for every 10 of nitrogen fixed. It was Krogh's view that the retia mirabilia may play a role. Campbell (*823*) 1934 advanced the theory that the whale avoids decompression sickness by filling the lungs with sea water when it submerges. There is no confirmation in the literature of this opinion. In fact, Gray (*827*) 1934 points out that the whale's blow-hole is designed to keep out the water. Gray refers to the possibility that the whale may avoid decompression sickness by short-circuiting the pulmonary circulation during submergence.

Damant (*824*) 1934 stated that at a depth of 100 m. (11 atmospheres (absolute)) the whale's alveoli might contract so as to present but one-eleventh of their surface volume at 1 atmosphere. According to Damant, this would tend to obstruct the diffusion of nitrogen into the blood and also favor discharge when the animal surfaces.

Diving mammals, as previously stated, are capable of more prolonged periods of submergence because of physiological adaptations by which the circulation is slowed, the metabolic rate reduced, and the oxygen requirement diminished. For a description of the respiratory characteristics of the blood of the seal, the reader should consult a report published in 1935 by Irving, Solandt, Solandt, and Fisher (*838*). The respiratory adjustments of the seal when diving are discussed by Irving, Solandt, Solandt, and Fisher (*839*) 1935–36. The relation of bradycardia to the diving ability of seals is discussed by Irving, Scholander, and Grinnell (*836*) 1941. These same authors in 1942 (*837*) reported reduction of metabolic rate in seals during diving. For other adaptations of seals relative to their capacity for remaining underwater, the reader should consult reports by Robinson (*848*) 1939; Grinnell, Irving, and Scholander (*829*) 1942; Irving, Scholander, and Grinnell (*837*) 1942; and Scholander, Irving, and Grinnell (*850*, *851*) 1942. Experiments of Irving, Scholander, and Grinnell (*835*) 1941 indicate that the heart rate is also slowed in the porpoise during diving. The respiratory rate of the porpoise during submergence was considered in a brief report by Parker (*847*) in 1932. Green and Redfield (*828*) 1933 have investigated the respiratory functions of the blood of the porpoise.

For a brief statement of muscle and blood hemoglobin in the dolphin the reader should consult a paper by Eichelberger, Fetcher, Geiling, and Vos (*825*) 1939. The submergence periods of the Florida manatee were investigated in 1922 by Parker (*846*). In experimental investigations on respiration and diving of the Florida manatee, Scholander and Irving (*849*) 1941 also reported a slowing of the heart. Koppányi and Dooley (*841*) 1929 found that apnea could be induced in the muskrat by wetting the nostrils and stretching the neck or dorsiflexing the head. There is a rise in blood pressure and slowing of the heart at the same time. These responses undoubtedly represent the mechanism by which the muskrat prepares for diving. Irving (*831*) 1936–37 studied the respiratory adaptations of the beaver in diving. In this animal, there is cardiac arrhythmia, a fall in blood pressure, and increased cerebral blood flow together with a diminution in flow of blood through the muscles. Irving (*832*) 1938 reported but little change in respiratory rate in the beaver and muskrat on inhalation of 10 percent carbon dioxide. Further studies on survival of animals without breathing have been reported by Irving (*830*) 1934 and Irving and Orr (*834*) 1935.

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831. Irving, L. The respiration of beaver. *J. cell. comp. Physiol.*, 1936–37 *9*:437–451. [P]

832. Irving, L. The insensitivity of diving animals to CO_2. *Amer. J. Physiol.*, 1938, *124:* 729–734. [P]

833. Irving, L. Respiration in diving mammals. *Physiol. Rev.*, 1939, *19:* 112–134. [P]

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836. Irving, L., P. F. Scholander, and S. W. Grinnell. Significance of the heart rate to the diving ability of seals. *J. cell. comp. Physiol.*, 1941, *18:* 283–297. [P]

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838. Irving, L., O. M. Solandt, D. Y. Solandt, and K. C. Fisher. Respiratory characteristics of the blood of the seal. *J. cell. comp. Physiol.*, 1935, *6:* 393–403. [P]

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840. Jolyet, F. Recherches sur la respiration des cétacés. *Arch. Physiol. norm. path.*, 1893, Sér. 5, *5:* 610–618. [P]

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844. Laurie, A. H. Some aspects of respiration in blue and fin whales. *Discovery Rep.*, 1933, *7:* 363–406. [P, M, B]

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B. DIVING BIRDS

The capacity of ducks to hold the breath depends in part upon a vagal mechanism. The time of submersion tolerated by ducks was reported by Richet (*862, 863*) 1894 and this investigator also discussed the influence of atropine upon asphyxia in the duck. Richet found that if the duck is given sufficient atropine to prevent slowing of the heart during diving, asphyxia supervenes more rapidly than usual in the submerged duck. Regarding the question of whether drugs which slow the heart would prolong the tolerance of the duck to submergence, Richet (*864*) 1898 found that digitalin gave no noticeable increase in tolerance. Moreover, the temperature of the water was of little importance in determining the total time of submergence. Richet found that ducks could be trained to survive immersion for periods of 12 to 17 minutes, whereas untrained ducks survived no longer than 4 min-

utes, 5 seconds to 8 minutes, 1 second (an average of 6 minutes). Ducks who were habituated to immersion kept the glottis closed whereas unhabituated ducks, after a certain length of time, opened the glottis and let water into the trachea. In a further study (*865*) 1898, Richet kept ducks under water for 22 minutes, 35 seconds as well as 20 minutes, 45 seconds; all animals survived. These figures indicate the maximum possible tolerance of ducks to immersion.

Richet pointed out that submersion initiated a reflex closing of the glottis as well as slowing of the heart. According to Langlois and Richet (*858*) 1898–99, resistance to asphyxia in ducks does not depend upon the quantity of circulating blood. Animals which had been one-fourth exsanguinated were found to be just as resistant to asphyxia as normal animals. The mechanism, according to these investigators, lies in the inhibitory effect of the actual contact with the water. They found that a duck dies in 7 minutes if the trachea is ligatured and the animal kept in the open air. However, if after tracheal ligature the duck is placed in water at 20° C., it survives for 16 to 25 minutes. In animals injected 1 hour previously with 10 mg. of atropine, death occurs about 5 minutes after immersion. For further studies on the resistance of ducks to asphyxia, the reader should consult reports by Richet (*866*) 1899 and Langlois and Richet (*857*) 1898. For studies on the slowing of the heart and metabolic rate of ducks in diving, reference is made to papers by Huxley (*853*, *854*) 1913 reporting that submersion apnea in the duck is a postral reflex.

According to Orr and Watson (*859*) 1913, the respiratory rate in the duck is accelerated by oxygen lack, whereas carbon dioxide tends to slow respiratory movements or produce apnea. Regarding postral apnea in the duck, the reader should consult a paper by Paton (*860*) published in 1913 on the relative influence of the labyrinthine and cervical elements in its production. The mechanism of slowing of the heart which accompanies postral apnea in the duck has been discussed by Koppányi and Dooley (*856*) 1928. The reader will also find a consideration of submergence and postral apnea in the swan in a paper by Paton (*861*) 1926–27. A comparison of the respiratory adaptations of ducks and chickens is to be found in a brief report published in 1926 by Guthrie (*852*).

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853. Huxley, F. M. On the reflex nature of apnoea in the duck in diving: I. The reflex nature of submersion apnoea. *Quart. J. exp. Physiol.*, 1913, *6:* 147–157. [P]

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860. Paton, D. N. The relative influence of the labyrinthine and cervical elements in the production of postural apnoea in the duck. *Quart. J. exp. Physiol.*, 1913, *6:* 197–207. [P]

861. Paton, D. N. Submergence and postural apnoea in the swan. *Proc. roy. Soc. Edinb.*, 1926–27, *47:* 283–293. [P]

862. Richet, C. La résistance des canards à l'asphyxie. *C. R. Soc. Biol. Paris*, 1894, *1:* 244–245. [P]

863. Richet, C. Influence de l'atropine sur la durée de l'asphyxie chez le canard. *C. R. Soc. Biol. Paris*, 1894, *1:* 789–790. [P]

864. Richet, C. De l'influence de l'éducation sur la résistance du canard à l'asphyxie. *C. R. Soc. Biol. Paris*, 1898, Sér. 10, *5:* 481–483. [P]

865. Richet, C. De la résistance des canards à l'asphyxie. *C. R. Soc. Biol. Paris*, 1898, Sér. 10, *5:* 685–686. [P]

866. Richet, C. De la résistance des canards à l'asphyxie. *J. Physiol. Path. gén.*, 1899, *1:* 641–650. [P]

C. FISH

Two papers on the influence of high pressures on fish published in 1873 by Paul Bert (*867*, *868*) may be consulted. Bert subjected fish in water to 11 atmospheres of oxygenated air.

These animals died in less than 20 hours. At pressures corresponding to 15 atmospheres of air, animals succumbed in 40 hours. In these cases, death was ascribed to oxygen poisoning. Fish rapidly decompressed from hyperoxygenated water showed gas bubbles in the blood and died.

The effects of high pressures upon other forms of marine life, including coelenterates, echinoderms, arthropods, and fish were investigated by Ebbecke (*870*) 1935. For other studies of the response of fish to high pressure, papers by Carbonnier (*869*) 1873 and Woodland (*872*) 1911 may be consulted.

Gorham (*871*) 1898–99 reported that fish do show air emboli on decompression from depths. Many fish when taken from the sea and kept in aquaria were found to develop a strange condition in which gas bubbles formed under the epidermis of the fins, within the eyes, and sometimes in the connective tissue under the orbits. In some cases, this latter tissue becomes so emphysematous that the eyeballs are forced out of the sockets. Gorham's report carries a photograph of a scup illustrating protrusion of the eyes. The disease was finally fatal. The emphysema is apparently not due to gas-producing bacteria since no organisms could be demonstrated either by smear or by culture. Gorham suggested that the disease was due to decompression for the following reasons: (a) The fish susceptible to the condition were mainly the deeper-level dwellers, shallow-water fish not being affected. (b) Exhausting the air above a tank of normal fish produced the condition within a few hours or minutes. (c) Confining affected fish under a pressure corresponding to 20 ft. of water cured them completely in a short while. Gorham suggested that when fish were taken to shallow-water aquaria, gas was freed from the blood and this was responsible for the condition. It seems quite possible that this disease in fish, as reported by Gorham, is a decompression phenomenon. The length of time that gas bubbles persist in animals after decompression is variable and not precisely known for all species but the emphysema to which Gorham has called attention may have originated from rapid decompression. In animals, post-orbital emphysema following decompression has not been generally observed. Gas in subcutaneous tissues in other areas has, however, from time to time, been noticed in both man and animals.

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868. Bert, P. Influence des hautes pressions sur les poissons. *Gaz. méd. Paris*, 1873, Sér. *4*, *28:* 244. [C, P]

869. Carbonnier, [ ]. De l'influence de la pression extérieure sur la vie des poissons et de la lumière lunaire sur la végétation aquatique. *Bull. Soc. Acclim.*, 1873, Sér. 2, *10:* 16–23. [C, P]

870. Ebbecke, U. Über die Wirkungen hoher Drucke auf marine Lebewesen. *Pflüg. Arch. ges. Physiol.*, 1935, *236:* 648–657. [P]

871. Gorham, F. P. Some physiological effects of reduced pressure on fish. *J. Boston Soc. med. Sci.*, 1898–99, *3:* 250–254.

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Biology of Very High Hydrostatic Pressures

In diving, caisson, and tunnel operations, we are concerned with raised air pressure. It is of importance in an understanding of the physiological and pathological actions of elevated atmospheric pressure to be familiar also with the action of pressure *per se* on tissues completely immersed in fluid, in which the complicating factor of gases is avoided. There is a considerable body of literature dealing with the effects of placing tissues or small animals in enclosed chambers completely filled with water and raising the hydrostatic pressure to high levels. For a review of the significant articles published in this field, the reader is referred to a report by Cattell (*878*) 1936. Cattell has pointed out that at very high hydrostatic pressures, fluids are compressed to some extent. For example, Parsons and Cook (*907*) 1911 found that a liter of water at 4° C. was compressed to a volume of 925 cc. at 2,000 atmospheres and to a volume of 870 cc. at a pressure of 4,500 atmospheres. As Bridgman (*873*) 1925 and Ebbecke (*889*) 1936–37 have shown, there are also changes in the viscosity of various fluids. Chemical reactions are stated to be accelerated by an increase in hydrostatic pressure and such properties of solutions as surface tension, etc., are also changed.

Raised hydrostatic pressures at high levels exert characteristic effects upon living tissue. Proteins, for example, are coagulated at pressures of 5,000 to 12,000 atmospheres and the uptake of water by gelatine gels is increased. Up to 6,000 atmospheres, there is little effect on enzyme action, whereas, above 10,000 atmospheres, the activity becomes greatly diminished. Digestive enzymes of animal origin are more resistant to raised hydrostatic pressure than plant enzymes. Galactose and ptyalin are only slightly influenced by very high hydrostatic pressures. The toxins of diphtheria and tetanus are destroyed by 13,500 atmospheres while the antitoxins are unaffected. A pressure of 700 atmospheres for a long period of time inhibits bacterial activity. It appears significant that the magnitude of pressure required to destroy bacteria is of the same order as that producing first perceptible clouding of protein solutions.

Protozoa cease activity at 400 to 600 atmospheres but no permanent harm is done to them even if the pressure is maintained for 1 or 2 days. At 400 atmospheres, amebae become spherical. Higher forms such as molluscs, echinoderms, etc., are inactivated by 400 to 600 atmospheres and are killed by pressures of 400 to 1,000 atmospheres if of sufficient duration. In some cases, an additional increase in pressure caused convulsive movements followed by inactivity. In experiments on flat fish, it has been shown that the oxygen consumption is increased by hydrostatic pressure up to 100 to 125 kg. per sq. cm. As the pressure was increased above this level, the metabolic rate fell and death occurred at a pressure of 150 kg. per sq. cm. Because of mammals' necessity for air, the effects of raised hydrostatic pressure cannot be measured on such animals.

Many studies have been carried out on the effects of raised hydrostatic pressure on isolated muscles. Volume changes correspond to those of liquids. The length of the muscle is decreased and there is evidence of increased viscosity. If raised hydrostatic pressures are

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maintained long enough, there is pronounced structural disorganization of the muscle fibers. Raised pressure may cause contraction in resting muscle and greater shortening of striated muscle when stimulated. Subjecting isolated nerve for 10 minutes to a hydrostatic pressure of 200 to 600 atmospheres results in histological damage and swelling of the fibers. Under moderate pressure, action potentials are increased, whereas, with higher pressure, the action potentials are lowered and the rate of conduction in nerves is slowed. If the pressures are not too extreme, changes observed in various tissues are reversible.

Regnard (*912*) in 1884 found that raised hydrostatic pressure caused an increase in weight of a frog's foot immersed in fluid. Regnard reported that isolated muscles subjected to hydrostatic pressures of 600 to 1,000 atmospheres showed a considerable increase in rigidity. This muscular rigidity was of such sudden onset and such magnitude as to break the limbs of the frog if the muscles were still attached to their origins and insertions. The superficial muscles were more severely affected than the deep muscles. It was found that the heart continued to beat when all other muscles became rigid. If a frog was surrounded by a watertight rubber sack and then subjected to raised hydrostatic pressures, there was no muscle rigidity or increase of weight. For this reason, Regnard considered that raised hydrostatic pressure increased the volume of muscle by absorption of water during exposure to pressure. Excess of water under such conditions acts as a poison within tissues.

Regnard and Vignal (*918*) 1884 also subjected isolated tissue such as epithelium, muscle, nerve, and connective tissue to a hydrostatic pressure of 600 atmospheres for periods of 10 minutes and 2 hours. Under such conditions, the mucous cells of the frog's esophagus were broken and ciliated cells swollen with fluid. Connective tissues were also distended. In deep muscles subjected to 600 atmospheres for 10 minutes, the transverse striations of the muscle fibers were less clearly marked than normal and the fibers were friable. In the superficial muscles, the transverse striations were usually absent after the action of raised hydrostatic pressures. In nerves subjected for 10 minutes to 600 atmospheres, the nodes of Ranvier stood out more clearly than normal and the sheath of Schwann was separated from the fiber. Red blood cells were destroyed in superficial vessels.

According to Regnard (*916*) 1886, contractility of frog muscle was lost at 200 atmospheres and at 400 atmospheres the muscles became rigid. The weight of all tissues increased. In 1887, Regnard (*917*) reported that at pressures above 400 atmospheres, animal protoplasm is compressed. On decompression, the tissues returned to their original volume and, in addition, since tissues take up fluids at high pressures, there was swelling. On the basis of his experiments, Regnard concluded that raised hydrostatic pressure does not paralyze muscle activity until a depth of about 4,000 meters below sea level has been reached. However, at 2,000 meters' depth, a marine animal would already be impeded in its movement. At high pressures, the duration of a muscle twitch is increased and the frequency of stimulation required to tetanize the muscle is reduced. For example, in one experiment a faradic stimulus with a frequency of 30 per second was required to tetanize the muscle, whereas at 300 atmospheres a stimulus frequency of 5 per second produced tetanus. At 1 atmosphere, the latent period of a frog muscle was reported as 1/100 second; at 300 atmospheres, the latency was 3/100 second.

Further studies on the effects of raised pressures on muscular contraction have been reported by Lombard (*904*) 1892 and Ebbecke (*884*) 1914. The latter worker found no change in the activity of nerve or muscle at pressures of 200 to 300 atmospheres. According to Cattell and Edwards (*879*) 1928, a pressure of 60 atmospheres increased the tension developed during contraction of isolated skeletal muscles.

Ebbecke and Hasenbring (*893*) 1935 subjected isolated muscles to pressures from 1 to 800 atmospheres and reported a shortening of the muscle. According to Ebbecke (*886*) 1935, high pressures resulted in tetanus. For a study on the action current in muscle and nerve, the

reader may consult a paper by Ebbecke and Schaefer (*894*) 1935.

Shortening of frog stomach muscle as a result of pressure of 50 to 800 atmospheres was reported in 1936 by Ebbecke (*887*). According to Romanes (*920*) 1886, hydrostatic pressures as high as 150 atmospheres produced no change in the rhythm or excitability of freshly excised frog or tortoise hearts.

Edwards and Cattell (*896*) 1928 subjected isolated frog, turtle, and dogfish hearts to 60 atmospheres. They found an increase in the amplitude of contraction, an acceleration of the heart, and a facilitating effect on auriculo-ventricular conduction. Other studies on the effects of high pressures on isolated heart muscle were reported by Edwards and Cattell (*897*) in 1930 and by Cattell (*877*) in 1935. Brown (*874*) 1931 carried out experiments in which he subjected isolated turtle heart muscle to a hydrostatic pressure of 1,000 to 6,000 lb. per sq. in. There was a prolongation of response and a decrease in the total tension developed.

Concerning the effects of raised hydrostatic pressure on the central nervous system, Ebbecke (*888*) 1936 reported convulsive clonic movements of the extremities in frogs when subjected to 50 to 250 atmospheres. For a report of effects of hydrostatic pressure on nerve action potentials, the reader is referred to a paper by Grundfest and Cattell (*902*) 1935.

Callery and Portier (*876*) 1910 investigated the effects of high pressure on osmotic phenomena in red blood cells. Fresh red blood corpuscles from defibrinated blood were placed in hypotonic, isotonic, or hypertonic solutions and compressed in a hydrostatic chamber. Hemolysis and electrical conductivity were estimated at various pressures. At hydrostatic pressures from 1 to 100 atmospheres, there was almost no hemolysis and it was not marked until pressures of 300 or over had been reached. Conductivity changes depended upon the concentration of the saline solution. With the hypotonic solutions, there was an increase in conductivity ascribed to electrolytes leaving the cells. In isotonic solutions, little change occurred on pressure, whereas in hypertonic solutions, the conductivity usually fell. According to Fontaine (*898*) 1927, pressures of 500 to 700 kg. per sq. cm. for 2 to 7 hours did not increase the volume of the red cells. This is contrary to Regnard's view that red cells take up fluid as a result of raised pressures.

The comparative compressibility of serum and red blood cells in the blood of the horse was discussed by Fontaine (*899*) 1927. Ebbecke and Zipf (*895*) 1939 found that a pressure of 2,000 atmospheres acting on drawn human blood delayed or prevented clotting. When coagulation did occur, the clot was not as firm as normal nor did it retract. For further studies on the imbibition of fluids by tissues under the influence of high hydrostatic pressure, the reader is referred to two reports by Fontaine (*900, 901*) published in 1927. Several papers by Regnard may be consulted: (a) on the effects of raised hydrostatic pressures on ferments, algae, marine organisms, and isolated muscle (*909*) 1884; (b) on the effects of high pressures at ocean depths on protozoan life as well as other marine animals (*910*) 1884; (c) on the movement of cilia (*911*) 1884; (d) on the survival of marine organisms (*913, 915*) 1884 and 1885; and (e) on the eggs of fish (*914*) 1885.

Ameboid movement is impaired at high hydrostatic pressures, according to Brown and Marsland (*875*) 1936 and Marsland and Brown (*906*) 1936. High hydrostatic pressures also affect the function of the luminous organs in insects, according to Dubois and Regnard (*883*) 1884 and Marsland (*905*) 1939 has reported on hydrostatic pressure effects upon dividing egg cells. The reader should also consult a report by Ebbecke (*892*) 1944 on the effects of high hydrostatic pressures up to 2,000 atmospheres. At 400 to 600 atmospheres, paramecia are paralyzed and fall to the bottom. If the pressure is lowered, these organisms return to normal activity. However, pressures of 1,000 atmospheres or over are lethal.

According to Ebbecke, the first reaction of peripheral nerve to raised hydrostatic pressures is an increase in irritability followed by loss of function which may be irreversible. In frog spinal preparations, reversible paralytic

effects were observed at 50 to 150 atmospheres. These changes became irreversible at 250 to 300 atmospheres. Cells exposed to raised hydrostatic pressure—paramecia, red blood cells, tissue cultures, etc.—showed characteristic microscopic changes after raised hydrostatic pressures. The cells tended to become rounded and the nucleus pyknotic. The cytoplasm was vacuolated and there was clumping or lysis of the cell contents. None of these changes was specific.

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901. Fontaine, M. Du mode d'action des fortes pressions sur les tissus. *C. R. Acad. Sci., Paris*, 1927, *184:* 1345–1347.

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909. Regnard, P. Recherches expérimentales sur l'influence des très hautes pressions sur les organismes vivants. *C. R. Acad. Sci., Paris*, 1884, *98:* 745–747. [P]

910. Regnard, P. Note sur les conditions de la vie dans les profondeurs de la mer. *C. R. Soc. Biol. Paris*, 1884, Sér. 8, *1:* 164–168. [P]

911. Regnard, P. Note relative à l'action des hautes pressions sur quelques phénomènes vitaux (mouvement des cils vibratiles, fermentation). *C. R. Soc. Biol. Paris*, 1884, Sér. 8, *1:* 187–188. [P]

912. Regnard, P. Sur la cause de la rigidité des muscles soumis aux très hautes pressions. *C. R. Soc. Biol. Paris*, 1884, Sér. 8, *1:* 310–311. [P]

913. Regnard, P. Effet des hautes pressions sur les animaux marins. *C. R. Soc. Biol. Paris*, 1884, Sér. 8, *1:* 394–395. [P]

914. Regnard, P. Influence des hautes pressions sur l'éclosion des oeufs de poisson. *C. R. Acad. Sci., Paris*, 1885, Sér. 8, *2:* 48–49. [P]

915. Regnard, P. Phénomènes objectifs que l'on peut observer sur les animaux soumis aux hautes pressions. *C. R. Soc. Biol. Paris*, 1885, Sér. 8, *2:* 510–515. [P]

916. Regnard, P. Action des hautes pressions sur les tissus animaux. *C. R. Acad. Sci., Paris*, 1886, *102:* 173–176. [P]

917. Regnard, P. Les phénomènes de la vie sous les hautes pressions. La contraction musculaire. *C. R. Soc. Biol. Paris*, 1887, Sér. 8, *4:* 265–269. [P]

918. Regnard, P. and W. Vignal. Des lésions que produisent sur les tissus animaux les hautes pressions. *C. R. Soc. Biol. Paris*, 1884, Sér. 8, *1:* 403–404. [P]

919. Roger, H. Action des hautes pressions sur quelques bactéries. *C. R. Acad. Sci., Paris*, 1894, *119:* 963–965. [P]

920. Romanes, G. J. Experiments with pressure on excitable tissues. *Proc. roy. Soc.*, 1886, *40:* 446–447. [P]

921. Anon. The biologic importance of pressure. *J. Amer. med. Ass.*, 1935, *104:* 2259–2260.

Microbiology, Immunology, and Embryology

In the preceding section, a number of reports on the effects of high hydrostatic pressure on bacterial growth have been cited. Raised atmospheric pressures also have been reported to impair the growth of microorganisms. For example, Certes and Cochin (*924*) 1884 reported on the effects of high pressure on fermentation and the action of yeast; and Chlopin and Tammann (*925*) 1903 described the effects of high pressure on the growth of micro-organisms. In 1926, Cleveland (*926*) suggested the use of oxygen under pressure for the destruction of protozoa, bacteria, molds, and yeast. He recommended this technique to kill silkworm parasites and parasites in fish. d'Arsonval (*928*) 1891 and d'Arsonval and Charrin (*929*) 1893 recommended the use of carbon dioxide under 50 atmospheres of pressure to destroy bacteria. Sabrazès and Bazin (*937*) 1893 referred to the sterilization of organic extracts by the d'Arsonval method of filtration under 50 to 60 atmospheres' pressure of carbon dioxide. The authors disagreed with d'Arsonval's proposal and reported that pressures of 90 or more atmospheres of carbon dioxide do not destroy staphylococci. The reader will find reference to the suggested use of carbon dioxide at a pressure of 50 atmospheres for 24 hours in the destruction of bacteria in milk and water by Hoffmann (*931*) 1906. Berghaus (*923*) 1907 described the action of carbon dioxide, oxygen, and hydrogen under various pressures upon bacterial growth. The reader will also find reference to the effect of air pressures of 75 atmospheres on bacteria as well as the effect of carbon dioxide and oxygen under pressure in a paper published in 1923 by Lorentz (*932*).

Bean and Porter (*922*) 1945 have recently reported experiments on the influence of oxygen at high pressure on malarial parasites. These investigators injected pooled duckling or chick blood with *plasmodium lophurae.* The blood was divided into test and control samples. Test samples were equilibriated with oxygen at high pressure and all samples then injected into normal chicks. Parasite counts were made 4 to 5 days later. When the test blood was exposed to oxygen at a pressure of 90 lb. per sq. in. for 4 hours before injection into the chicks, the test blood showed an infectivity of one-tenth that of control blood. Test blood kept at 90 lb. per sq. in. gauge pressure for 6 hours before injection into chicks failed to induce any appreciable infection with the parasites. Exposure to oxygen at 45 lb. pressure for 6 and 12 hours did not completely eliminate infectivity of test blood but exposure to an oxygen pressure of 30 lb. per sq. in. for 3 hours caused a definite decrease in infectivity. An oxygen pressure of 30 lb. for 12 hours destroyed the infectivity of the test blood. In test blood samples exposed to oxygen pressure of 15 lb. per sq. in. for 3, 6, 12, and 24 hours, there was a progressive decrease in infectivity. The average parasite count following the 24-hour exposure of test blood was 5 organisms for every 10,000 red blood cells, whereas the control count was 2,100 per 10,000 cells. The parasites were found to be more resistant in duckling than in chick blood. Attempts to lower the parasite counts of chick blood *in vivo* by successive exposure of injected chicks to oxygen at a

pressure of 90 lb. per sq. in. for 4-minute periods were indecisive because of the high susceptibility of these birds to the toxic action of the oxygen.

Marsh (*933*) 1931 kept cancer-susceptible mice in compressed air at 3 atmospheres for prolonged periods. The experimental mice were reported to be in better physical condition than the control animals. Breeding was normal and a slight reduction in tumor incidence was claimed.

For a study of the effect of compressed air on anaphylactic shock, the reader is referred to a report published in 1933 by Polettini (*935*). In 1933, Severi (*938*) reported on the influence of compressed air on the production of agglutinins in animals, and Polettini (*936*) 1933 described the influence of compressed air on sensitization of animals to anaphylactic shock and histamine shock. Severi (*939*, *940*) 1834 described the effect of compressed air on hemolysins and on the titer of complement. According to Severi (*941*) 1935, compressed air at a pressure of 6 atmospheres (absolute) inhibits the formation of agglutinins and precipitins during immunization. When these antibodies are already formed, a pressure of 6 atmospheres exerts no effect. Raised atmospheric pressures exert no influence on the formation of hemolytic antibodies. Raised atmospheric pressures, according to Severi, act only upon the cell elements which form agglutinins and precipitins and a pressure of 6 atmospheres was found to have no effect on the titer of complement. According to Piery, Ponthus, and Meyer (*934*) 1936, low pressure runs did not appear to have any effect on the production of anaphylactic shock in guinea pigs sensitized by injections of horse serum.

For a consideration of the effect of high pressures (8 to 18 lb. per sq. in.) on the incubation of chick embryos, the reader should consult a paper by Cunningham (*927*) 1926–27.

922. Bean, J. W. and R. J. Porter. Influence of O_2 at high pressure on malarial parasites. *Fed. Proc. Amer. Soc. exp. Biol.*, 1945, *4:* 6. [M]

923. Berghaus, [ ]. Über die Wirkung der Kohlensäure, des Sauerstoffs und des Wasserstoffs auf Bakterien bei verschiedenen Druckhöhen. *Arch. Hyg., Berl.*, 1907, *62:* 172–200.

924. Certes, A. and D. Cochin. Action des hautes pressions sur la vitalité de la levure et sur les phéromènes de la fermentation. *C. R. Soc. Biol. Paris*, 1884, Sér. 8, *1:* 639–640.

925. Chlopin, G. W. and G. Tammann. Ueber den Einfluss hoher Drucke auf Mikroorganismen. *Z. Hyg. InfektKr.*, 1903, *45:* 171–204.

926. Cleveland, L. R. Some problems which may be studied by oxygenation. *Science*, 1926, *63:* 168–170. [P]

927. Cunningham, B. The incubation of hen eggs under increased atmospheric pressure. *J. Elisha Mitchell sci. Soc.*, 1926–27, *42:* 188–192, 1 pl.

928. d'Arsonval, A. Emploi de l'acide carbonique liquéfié pour la filtration et la stérilisation rapides des liquides organiques. *C. R. Acad. Sci., Paris*, 1891, *112:* 667–669. [P]

929. d'Arsonval, [ ] and [ ] Charrin. Pression et microbes. *C. R. Soc. Biol. Paris*, 1893, Sér. 9, *5:* 532–534. [P]

930. Greenwood, M., Jr. The effects of rapid decompression on larvae. *J. Physiol.*, 1906–07, *35:* vi. [P]

931. Hoffmann, W. Über den Einfluss hohen Kohlensäuredrucks auf Bakterien im Wasser und in der Milch. *Arch. Hyg., Berl.*, 1906, *57:* 379–400. [P]

932. Lorentz, F. H. Die veränderung von Bakterien unter Gasen. *Klin. Wschr.*, 1923, *2:* 206–208.

933. Marsh, M. C. Tumor strain mice in compressed air. *Amer. J. Cancer*, 1931, *15:* 2252–2264.

934. Piery, A., P. Ponthus, and P. Meyer. De l'influence de la dépression atmosphérique en caisson sur l'apparition du choc anaphylactique. *C. R. Soc. Biol. Paris*, 1936, *121:* 691–693. [P]

935. Polettini, B. Azione dell'aria compressa sugli animali. IV. Influenza sullo shock anafilattico. *Boll. Soc. ital. Biol. sper.*, 1933, *8:* 82–87. [P]

936. Polettini, B. Azione dell'aria compressa sugli animali. VII. Influenza sulla sensibilizzazione anafilattica e sullo shock istaminico. *Boll. Soc. ital. Biol. sper.*, 1933, *8:* 173–176. [P]

937. Sabrazès, J. and E. Bazin. L'acide carbonique à haute pression, peut il être considéré comme un antiseptique puissant. *C. R. Soc. Biol. Paris*, 1893, Sér. 9, *5:* 909–912. [P]

938. Severi, R. Azione dell'aria compressa sugli animali. VI. Influenza sulle agglutinine. *Boll. Soc. ital. Biol. sper.*, 1933, *8:* 170–173. [P]

939. Severi, R. Azione dell'aria compressa sugli animali. XIV. Influenza sulle emolisine. *Boll. Soc. ital. Biol. sper.*, 1934, *9:* 528–530. [P]

940. Severi, R. Azione dell'aria compressa sugli animali. XV. Influenza sul potere complementare. *Boll. Soc. ital. Biol. sper.*, 1934, *9:* 530–533. [P]

941. Severi, R. Azione dell'aria compressa sui processi immunitari. Ricerche sperimentali. *Boll. Ist. sieroter., Milano*, 1935, *14:* 419–430. [P]

Effects of High Pressures on Plant Growth

Two papers on the effect of raised atmospheric pressures on the growth of plants are included for completeness. The first is that of Paul Bert (*942*) published in 1873 in which the great French physiologist reported that the germination of grains was slowed and finally arrested under a pressure of 8 to 10 atmospheres. Plants subjected to a pressure of 7 to 8 atmospheres were lethally affected, according to a report by Bordier (*943*) 1877.

In Bert's experiments, cereal grains subjected to pressures of 8 to 10 atmospheres were killed by these pressure levels and did not germinate when subsequent attempts were made to grow them at sea-level pressure. Bert believed that the deleterious action of compressed air on the germination of grains was due specifically to the effect of oxygen under high pressure. Pure oxygen at pressures of 3 or 4 atmospheres had a more lethal effect on the germination of cereal grains than did oxygen-poor air under the same pressures.

Bert found that the grains of cereals are more sensitive to the action of high pressures than are the grains of the Cruciferae, so that the latter germinated at air pressures at which cereal grains were killed. The greater susceptibility of the grains of cereals to high pressure was related by Bert to the effect of high pressures on alcoholic fermentation within the grains. At atmospheric pressure, the germination of cereal grains takes place less readily in an atmosphere of pure oxygen than in ordinary air. Bert found that air containing 30 to 40 percent oxygen at atmospheric pressure afforded optimum conditions for growth.

Bordier's paper consists of a discussion of the theory, current at the time (1877), that during early geologic periods the atmospheric pressure was higher than at present. Bordier believed that there has been a progressive diminution in the weight of the atmosphere and that this factor has influenced the evolutionary process in determining the changes that living organisms have undergone throughout the various epochs. Bordier briefly reviewed the development of the organ of hearing and suggested that the simpler auditory apparatus of lower animals was an adequate adaptation for hearing in a denser atmospheric medium whereas in the case of higher animals a more complicated organ was developed to meet the more exacting needs of reception of sound waves transmitted through a rarer medium.

Bordier considered it possible that the mechanism of breathing by gills is an adaptation that developed during an epoch of higher oxygen pressure than at present. Similarly, the three-chambered heart of reptiles and lower animals in which there is a mixing of arterial and venous blood in the ventricle, was seen as an anatomical mechanism of survival value at higher atmospheric pressures than prevail at present.

Bordier asserted that the effects of compressed air on vegetation also plead in favor of the hypothesis of a higher atmospheric pressure in earlier geologic times. Bordier quoted experiments indicating that the germination of seeds is enhanced by pressures up to 2 or 3 atmospheres. Above 4 or 5 atmospheres, germination is retarded, especially for cereal grains. Vegetation in early geologic epochs was composed of plants not of the cereal type.

It was Bordier's contention that only such vegetation existed as was able to withstand the higher atmospheric pressure then prevailing.

Bordier stated that before the appearance of plants on the earth's surface, pressures of more than 7 to 8 atmospheres may have existed. Under such conditions, life in the form of organized living structures was precluded although various fermentation reactions may have been possible.

942. Bert, P. Sur l'influence des modifications dans la pression atmosphérique. *Gaz. méd. Paris*, 1873, Sér. 4, *28:* 66–67. [C, P]

943. Bordier, A. De l'influence de la pression atmosphérique sur l'organisme aux temps préhistoriques et de son rôle transformiste. *Bull. Soc. Anthrop. Paris*, 1877, Sér. 2, *12:* 109–114.

Diseases and Accidents in Submarine Personnel, Divers, and Compressed Air Workers

I. DISEASES AND ACCIDENTS IN SUBMARINE PERSONNEL

Reference is made throughout this Sourcebook to medical and surgical conditions which may be encountered in submarine personnel during patrols and on return from patrols. These conditions are discussed in the following reports.

944. Belli, C. M. and G. Olivi. Crasi sanguigna, respirazione e circolazione nei sommergibili immersi. *Ann. Med. nav. colon.*, 1913, *2:* 457–469.

945.* Bianchi, G. Saggi di fisiopatologia dei sommergibilisti. *Ann. Med. nav. colon.*, 1941, *47:* 283–359.

946. Brown, E. W. Submarine division five. *Nav. med. Bull., Wash.*, 1919, *13:* 846–853. [R]

947. Chevalier, [ ]. Brûlures assez étendues causées par une explosion de gaz dans la chambre de déseclusement aux travaux de l'air comprimé pour la construction du pont de Cubzac. *Rev. sanit. Bordeaux*, 1883–84, *1:* 121–122.

948. Comte, L. Rapport sur l'explosion d'un cylindre à air comprimé sur l'avaleresse no 7, dite la Naville, située dans la concession de Douchy (Nord). *Ann. Min., Paris*, 1847, Sér. 4, *11:* 121–148. [C]

949. Crecchio, G. de. Sulle lesioni presentate dai cadaveri dei marinai periti per lo scoppio del sommergibile "Foca". *Tommasi*, 1913, *8:* 297–301. [P]

950. Cress, W. W. Effects of submarine duty on personnel. *Milit. Surg.*, 1917, *40:* 699–709. [R]

951. Hall, R. W. B. Eye-strain in the submarine service. Notes on the symptoms, causation, treatment, and prevention of the condition. *J. R. nav. med. Serv.*, 1919, *5:* 180–183. [R]

952. Halsey, W. H. The submarine: its casualties in peace and war. *Milit. Surg.*, 1916, *38:* 50–55. [R]

953. Lafolie, [ ]. Tension artérielle et plongées sous-marines. *Arch. Méd. Pharm. nav.*, 1919, *108:* 108–110. [P]

954. Layet, [ ]. Hygiène des plongeurs. *Rev. sanit. Bordeaux*, 1886, *4:* 67–70; 85–88; 108–110.

955. Lindemann, [ ]. Die Krankheiten der Bergleute und Tunnelarbeiter. Pp. 1–32 in: *Handbuch der Arbeiterkrankheiten.* Edited by Theodor Weyl. Jena, Gustav Fischer, 1908, lxix, 809 pp. [R]

956. McDowell, R. W. Diseases incident to submarine duty. *Nav. med. Bull., Wash.*, 1917, *11:* 44–50. [R]

957. Thibaut, L. and L. de Méricourt. Note sur les accidents observés pendant l'usage d'un scaphandre, dont le tuyau injecteur d'air, en caoutchouc vulcanisé, venait d'être renouvelé. *Arch. Méd. Pharm. nav.*, 1864, *1:* 225–239. [R]

958. Van Der Aue, O. E. and V. R. Cullen. Gingivitis among submarine personnel. *Nav. med. Bull., Wash.*, 1945, *44:* 811–816. [M]

II. EAR, NOSE, AND THROAT DISTURBANCES

Ear symptoms occurring as a result of failure to equalize pressure within the middle ear during compression do not belong under the classification of decompression sickness. On the other hand, decompression, if too rapidly carried out, may be a cause of otological disturbances which may be considered a part of the symptom complex "decompression sickness." For convenience, all ear, nose, and throat disturbances caused by work in compressed air are grouped in this section. In attempting to classify the literature in this section, one might divide the reports into those dealing with difficulties of (a) the external ear, (b) the middle ear, (c) the internal ear, and (d) the sinuses, etc.; or, abandoning an anatomical classification, one may consider the literature under the headings: (a) compres-

sion accidents, and (b) decompression disturbances. The latter plan of classification has been adopted. However, classification of the literature is somewhat complicated by the fact that it has only been within the last few years that two distinct types of ear damage have been clearly recognized: (a) damage caused by faulty equalization of pressure, and (b) damage caused by decompression.

For the most part, the disturbances occurring during compression are localized within the middle ear and are associated with failure to equalize pressure. Carillon (*970*) 1900 also listed disturbances of the external auditory canal under complications arising during compression and noted that compression resulted in hypersecretion of glands of the external auditory canal. Disturbances of the middle ear included congestion of the tympanum and retraction or rupture of the membrane. There might also be hemorrhage in the middle ear. According to Carillon, middle ear disturbances arising during compression may be transmitted to the internal ear. He also noted vertigo in some cases during compression. However, compression effects were rarely incapacitating, and once workmen had been able to clear their ears, there were usually no other aural symptoms while working at pressure. Carillon listed as decompression symptoms vertigo, deafness, and tinnitus. The middle ear or sinuses might become blocked during decompression, but ordinarily, because of the valve-like action of the pharyngeal opening of the Eustachian tube, there was usually no difficulty in expelling air from the middle ear during reduction of pressure.

As stated, the literature in this section will be discussed under two main headings: (a) disturbances arising during compression, and (b) difficulties experienced as a result of decompression. A number of early papers consider both classes of effects and these will be described first. A few reports primarily concerned with auditory acuity in compressed air workers are listed at the end of the section.

A. GENERAL STUDIES OF OTORHINOLARYNGOLOGICAL DISTURBANCES

Classic observations on ear disturbances resulting from compressed air work were carried out by Alt (*961*) 1897 and Alt, Heller, Mager, and von Schrötter (*962*) in 1897. For 2 years, Alt worked in conjunction with Heller, Mager, and von Schrötter studying the workers in the caisson at Nussdorf. With regard to the effects of rise of pressure, Alt recognized that pain in the ears was due to failure to open the Eustachian tube. He called attention to great individual variation in toleration of pressure changes but believed that the healthy ear should withstand a compression rate of at least 1/10 atmosphere per 1½ minutes. If the compression rate was too rapid, there was dullness of hearing and a sense of the ear drum being drawn inward. As the pressure increased, the patient might hear a sudden sharp, short crack associated with opening of the Eustachian tube. Pains due to an excessively rapid compression rate ordinarily ceased when the pressure became stationary. While working in the caisson under pressure, therefore, workmen did not usually complain of symptoms referable to the ears and, according to Alt, there was no loss of auditory acuity although Smith (*76*) 1873, Clark (*1373*) 1870–71, and Pol and Watelle (*75*) 1854 all claimed that hearing is poor in the caisson. It has been claimed that transmission of sounds is enhanced in compressed air and that, provided the drum is normal, sounds are heard better. There are many allusions in the early literature to temporary improvement of auditory acuity in partially deaf workmen while in the pressure chamber. Workmen noticed voice changes at about 1.5 atmospheres (absolute). At 3.5 atmospheres (absolute) the voice had a silvery clear, metallic sound. On decompression, there might sometimes be partial deafness and the subject might hear sounds in the ear due to the outflow of air from the Eustachian tube.

Alt stated that divers usually have a feeling of deafness after an ascent. This ordinarily lasted for only a few hours, but symptoms might persist for days. Alt found that the fog appearing during decompression made it difficult to examine the ear drum properly in spite of electric lights. He did claim that the drum might be affected but pointed out that

decompression was much less troublesome to the ear than compression. During compression, middle ear disturbances might be alleviated and the pressure equalized by swallowing or by the Valsalva maneuver. According to Alt, the labyrinth might also be involved in compression effects on the middle ear and evidence was cited to show that rarefaction or compression of the air in the middle ear results in corresponding changes of pressure in the labyrinth. There might also be stasis, transudation, or even hemorrhage within the labyrinth. Because of these difficulties, Alt recommended that divers should not descend or ascend at a more rapid rate than 2 m. per minute. He called attention to ecchymosis or rupture of the ear drum, hemorrhage in the middle ear, or acute otitis media.

Alt believed that gas emboli might be liberated in the inner ear, producing obstruction of labyrinthine vessels and resulting in various ischemic or hemorrhagic lesions. Alt stated that after decompression there might be a rise in systolic blood pressure. This might increase the congestion and stasis in the middle ear.

Shortly after decompression, workers were sometimes seized with sudden vertigo, vomiting, and buzzing in the ears. The patient would stagger as if intoxicated and complain of noise in the ears, or there might be collapse with or without unconsciousness. The patient was usually confined to bed for days chiefly because of the vertigo. Improvement followed in cases where there was presumably only ischemia in the internal ear. In some instances, however, the patient was left with a permanent auditory defect which was considered due to hemorrhage resulting in destructions of nerve structure within the auditory apparatus. Vertigo might also persist although this symptom usually regressed. Alt reported three typical cases of labyrinthine disease in caisson workers as well as nine cases with well-developed Ménière's symptoms.

In experiments on animals, Alt produced ecchymosis of the ear drum and hemorrhage within the middle ear by rapid compression to 2.2 atmospheres (absolute). Guinea pigs, rabbits, and dogs were decompressed within ½ to 1 minute from a pressure level of 4 atmospheres. The bulla was filled with a dark brown, coagulated mass and, on histological examination of the labyrinth, the vessels of the modiolus of the cochlea were filled with erythrocytes and were surrounded by perivascular extravasations. In places, the cochlear nerve was seen to be lifted away from the bone by hemorrhage. Some extravasation of blood was observed in various parts of the scala tympani and the scala vestibuli. However, the vestibule was for the most part free of hemorrhage while in the semicircular canals, both in the membranous and bony portions, there were definite hemorrhagic extravasations.

Middle and inner ear disturbances were also referred to in 1895 by Heller, Mager, and von Schrötter (*975*), and Friedrich and Tauszk (*971*) in 1896 also reported aural pain on "locking in" and on "locking out" of caissons. In one case reported by Friedrich and Tauszk, there was pain in the ears accompanied by vertigo lasting from 10 to 14 days. For a comprehensive review of the early observations on ear disturbances in divers and caisson workers, the reader should consult papers published in 1900 by Baratoux (*964*, *965*). These reports refer to descriptions of ear pains in divers or compressed air workers by several early investigators. Baratoux listed the working depths in various constructions and also reviewed case histories and the theories of the etiology of the labyrinthine lesions. Regarding the pressure effects on the middle ear and the ear drum, Baratoux stated that retraction of the drum was noticeable at a pressure of 1.5 atmospheres (absolute).

Three cases of ear involvement in caisson workers were reported in 1900 by Tomka (*986*). In the first case, there was dizziness, shivering, pain in the extremities, and diminished hearing. The left ear drum was inflamed. The second patient complained of dizziness, noises in the ear, and pain in the extremities. There was partial deafness in the left ear and the drum on that side was retracted and congested. There was also congestion in the right ear drum. In the third case, there were pains in the extremities and sternum and the

right ear drum was perforated. Hearing, however, was normal.

In 1901–3, Heermann (*974*) described observations on the effects of compressed air on the ear in connection with the construction of the foundations of the docks in the harbor at Kiel. Cases of otitis media and difficulty of hearing were described. Heermann believed that Ménière's symptoms were due to ischemic lesions in the labyrinth occurring as a result of decompression.

In 1907, Philip (*981*, *982*) reported his experiences with aural disturbances in caisson workers employed in the construction of a metropolitan railroad bridge in Paris. A worker of 28 years of age complained of tinnitus, vertigo, earache, and bleeding from the left ear on entry into the caisson. These symptoms were so severe that he was forced to leave. Several days later, hearing was normal in the right ear but air conduction was diminished on the left side. The right ear drum was red and somewhat swollen, whereas the left drum was hemorrhagic. The pain and vertigo had disappeared. A worker at Passy experienced violent pain in the left ear on "locking in" which was not helped by the Valsalva maneuver. He had nose bleed also but continued to work for 8 hours in the caisson. Following this, there was total deafness in the left ear with pain and tinnitus for 15 days. Air conduction was abolished in the left ear but bone conduction was normal. The hearing was normal in the right ear and on speculum examination showed no abnormalities. However, the left tympanum was swollen and mobile and the promon tory was hyperemic. A polypoid obstruction was found in the left nasal passage. Regarding prognosis, Philip believed that in those cases in which the external and middle ear only were affected, good progress was usually to be expected. However, there might be some residual hearing loss. In the case of labyrinthine involvement, the prognosis could not be established so early. If, at the end of 1 month, deafness was still total and bilateral, the disability should be considered permanent from a medicolegal point of view. If the patient was left with a permanent Ménière's syndrome, he should be considered totally incapacitated and should receive compensation accordingly.

In 1908, Berruyer (*967*) reported on accidents to the ears occurring during "locking in" or "locking out" in the course of construction work on the piles for a bridge over the Seine. He pointed out that either the middle or inner ear was primarily affected but that there might be bleb formation or subcutaneous emphysema in the outer ear. Compression and decompression disturbances associated with failure to equalize the pressure in the middle ear were discussed. Berruyer also considered that on "locking in," failure to equalize pressure in the middle ear may also indirectly affect the labyrinth. Signs and symptoms, as well as diagnosis, prognosis, treatment, and prophylaxis were described.

In 1913, Boot (*968*) described several cases of "blocked" ears. Most of these patients were experienced workmen who had worked for many years in compressed air. Most cases showed pathological changes in the ear drums as well as diminished auditory acuity or complete deafness in 1 or both ears. Out of 155 cases of caisson disease referred to by Koelsch (*976*) in 1915, 1 complained of dizziness and a feeling of pressure in the ear. Thost (*984*) 1921 described dizziness and disturbances of equilibrium in some patients and reported X-ray evidence of gas bubbles within the mastoid process.

For a more recent study of ear disturbances in compressed air workers, the reader may consult the report by Korte (*977*) published in 1933. For the most part, this article is a review of the work of Alt, Heller, Mager, von Schrötter, and other workers. A case history of a patient seen by Korte is given. This patient had previously had hemorrhages in both ears on "locking out" of caissons and, in 1931, experienced severe headache and inability to equalize the pressure on entering the caisson. After leaving the caisson, he was unable to walk properly and finally collapsed. On examination, he showed slight diminution in auditory acuity and turbidity in both ear drums. He was able to walk only with the aid of a stick. These symptoms were brought on

presumably by compression as well as decompression.

Thost (*985*) 1928 emphasized the danger of rupture of vessels of the ear as a result of too rapid pressure changes. The tympanum was a particularly susceptible site of injury and Thost recognized the danger of damage to central nervous structures such as the auditory nerve as a result of bubble formation. These injuries occurred only when the atmospheric pressure varied too rapidly. Clinical observation as well as animal experiment demonstrated that aural tissues could withstand changes in pressure if these were carried out slowly enough. Thost also reviewed the work of Khrabrostin (*1090*) in 1888 who reported cases of dizziness, weakness, dyspnea, lameness of extremities, hemorrhage, ecchymosis, and inflammation of the ears. Khrabrostin also called attention to deafness or dullness of hearing, either bilateral or unilateral, lasting only a few hours or enduring a few days. Tinnitus in Khrabrostin's experience was an unusual symptom. Reference may also be found in Thost's paper to observations of Catsaras (*1236*) 1890 who recorded noises in the ears, dizziness, vertigo, loss of consciousness, motor aphasia, deafness, and blindness as results of too rapid decompression of divers. The report of Thost is also of interest to readers concerned with high altitude physiology as it pertains to aural function because it gives an account of lesser known facts about ear involvement in the balloon flights of Croce-Spinelli, Sivel, and Tissandier. Ear involvement was also noted in mountain climbers and in others attempting balloon ascents. Reference was made to ear disturbances which may occur in caisson workers on "locking in" and particularly to the semi-permanent or permanent changes in the inner ear which may follow too rapid alteration of pressure.

Thost differentiated the following types of injury to the ear in compressed air work: (a) Direct injury due to pressure and not to gas emboli (in 9 cases out of the group of 112) occurring on "locking in" or shortly thereafter. These were characterized by pain, noises in the ear, and difficulty in hearing. In the majority of these cases, the condition arose from an inability of the subject to equalize pressure because of congestion of the Eustachian tube or because of previous ear injuries. (b) The effect of air pressure upon other fossae or tubes in the body which connect with the external ear such as the sinuses, eyes, lungs, etc. Sinusitis arising from difficulty in equalizing air pressure was considered to be a very serious complication. (c) The effect of pressure on the vestibular apparatus. In these cases, medical officers might encounter such symptoms as vertigo, noises in the ear, and vomiting. According to Thost, these symptoms might occur with no visible changes whatever in the middle ear, and it was generally agreed that they were probably due entirely to effects on the inner ear. As symptomatologic of gas emboli in the inner ear, Thost listed noises in the ear, vertigo, and collapse. There may also be unilateral deafness which is frequently permanent.

According to Bornstein (*390*) 1914, 76.7 percent of all cases of caisson disease recover completely. However, compressed air workers are left with serious residual disabilities and one of these may be unilateral or even bilateral deafness. This deafness may be partial or complete. Thost (*984*) 1921 referred to dizziness in caisson workers associated with disturbance of equilibrium due to gas bubbles in the vessels of the petrous portion of the temporal bone. Thost demonstrated bubbles in the mastoid process by X-ray. Korte (*977*) in 1933 also reported involvement of the ears in caisson disease and called attention to the fact that "locking out" of the caisson was ordinarily less painful than the process of "locking in."

Manigan (*979*) in 1939 referred to Boot's classification of loss of hearing in caisson disease under three headings: (a) tubal tympanic catarrh, (b) symptoms referable to the vestibular system, and (c) loss of hearing in the upper range with disturbances of bone conduction. He reviewed other workers' observations on laceration of the ear drums and deafness due to caisson disease and also considered etiological factors in aural manifestations of decompression sickness. In laboratory preparations, he reported that

bubbles tend to form in the inner ear, altering the contour of structures or tearing tissues. In the inner ear, vascular stasis and hemorrhage were observed.

A brief summary of aural disturbances in compressed air workers was given by Almour (*959*) in 1942. This author considered three types of labyrinthine involvement resulting from faulty decompression: (a) transient auditory and vestibular symptoms; (b) symptoms of inner ear involvement including vertigo, tinnitus, headache, and deafness due to damage to the auditory nerve, which symptoms may recede very slowly with eventual recovery; and (c) symptoms characteristic of inner ear involvement from which the patient does not show appreciable recovery, and leaving a permanent impairment of cochlear or vestibular function, or both. Almour stressed the importance of the condition termed "blocked ear." He pointed out that any disturbance to the drum or middle ear may be included under this term and that the condition is caused by tubal occlusion which prevents equalization of pressure in the middle ear. Almour differentiated 2 degrees of the condition; in the first, there is retraction of the tympanic membrane together with hyperemia. In the second degree, there is hemorrhage within the middle ear and retraction or perforation of the ear drum. There may or may not be free hemorrhage into the external auditory meatus. A study of 55 cases of "blocked ear" revealed acute hearing loss in all individuals. Where the drum was not perforated, the condition yielded rapidly to diathermy or shortwave therapy. Almour discussed the forensic aspects of otological problems in caisson workers and suggested the need for a regularized procedure for estimation of hearing loss in such workers. In the discussion following Almour's paper, Jackson described the use of a helium-oxygen gas mixture to relieve blocked ears.

For other articles concerned with general otological aspects of compressed air illness, the reader is recommended to consult reports by the following authors: Philip (*981*) 1907, Grant (*973*) 1908, Thost (*983*) 1921, Malan (*978*) 1934, Alonzo (*960*) 1938, Anthony (*963*) 1939, and Gandino (*972*) 1940.

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960. Alonzo, P. Igiene e patologia dei palombari. (Rivista sintetica). *Difesa soc.*, 1938, *17:* 1045–1076.

961. Alt, F. Pathologie der Luftdruckerkrankungen des Gehörorgans. *Verh. dtsch. otol. Ges.*, 1897, *6:* 49–64. [P]

962. Alt, F., R. Heller, W. Mager, and H. von Schrötter. Pathologie der Luftdruckerkrankungen des Gehörorgans. *Mschr. Ohrenheilk.*, 1897, *31:* 229–242. [P]

963. Anthony, D. H. A review of the literature on injuries to the eyes, ears, and sinuses, and a summary of seventy cases treated. *Memphis med. J.*, 1939, *14:* 76–79. [R]

964. Baratoux, J. Des accidents suriculaires dans l'air comprimé. *Prat. méd., Paris*, 1900, *14:* 33–39; 49–57. [R]

965. Baratoux, J. Des accidents survenant du côté de l'oreille dans l'air comprimé. *Indép. méd., Paris*, 1900, *6:* 114. [R]

966. Behnke, A. R. Physiologic effect of pressure changes with reference to otolaryngology. *Arch. Otolaryng., Chicago*, 1945, *42:* 110–116. [M]

967. Berruyer, [ ]. Les accidents auriculaires chez les travailleurs des caissons. *Bull. méd., Paris*, 1908, *22:* 607–610. [P, R]

968. Boot, G. W. Caisson workers' deafness. *Ann. Otol., etc., St Louis*, 1913, *22:* 1121–1132. [P, Ch]

969. Campbell, P. A. Progress of aviation otology in World War II. *Arch. otolaryng. Chicago*, 1945, *41:* 381. [R, M]

970. Carillon, E. *Troubles de l'oreille dans l'air comprimé* Thèse (Méd.) Paris, Imprimerie A. Malverge, 1900, 80 pp. [P, R]

971. Friedrich, W. and F. Tauszk. Die Erkrankung der Caissonarbeiter (Caissonkrankheit). *Wien. klin. Rdsch.*, 1896, *10:* 233–235; 249–250; 267–268; 287–288; 323–324.

972. Gandino, D. La malattia dei cassoni dal punto di vista otoiatrico. *Rass. Med. Lav. industr.*, 1940, *11*: 142–148. [R]

973. Grant, C. G. A few cases of compressed-air illness with remarks. *Brit. med. J.*, 1908, *1*: 1567–1568. [Ch]

974. Heermann, G. Über Caissonkrankheit. *Samml. klin. Vortr.*, 1901–03, No. 81–101; 385–404. [R]

975. Heller, R., W. Mager, and H. von Schrötter. Vorläufige Mittheilung über Caissonarbeiter. *Wien. klin. Wschr.*, 1895, *8*: 475–476. [P, R]

976. Koelsch, F. Arbeiten in Pressluft. *Zbl. Gew-Hyg.*, 1915, *3*: 61–66; 81–85. [P, Ch]

977. Korte, J. Über die Beteiligung des Ohres bei der Caissonkrankheit. *Z. Laryng. Rhinol.*, 1933, *24*: 349–358. [R, Ch]

978. Malan, A. L'orecchio nei palombari. *Ann. Med. nav. colon.*, 1934, *40*: 8–24.

979. Manigan, T. P. Otologic aspect of caisson disease. *Memphis med. J.*, 1939, *14*: 81–84. [R]

980. Miller, N. F. An interpretation and evaluation of tubal patency tests. *J. Amer. med. Ass.*, 1945, *129*: 243–246. [R]

981. Philip, M. Des accidents auriculaires chez les travailleurs des caissons. *Ann. Mal. Oreil. Larynx.*, 1907, *33*(1): 140–158. [R]

982. Philip, M. Des accidents auriculaires chez les travailleurs des caissons. *Gaz. hebd. Sci. méd.*, 1907, *28*: 206–212. [R, Ch]

983. Thost, [ ]. Die Caissonerkrankungen beim Bau des Hamburger Elbtunnels. Nach einem auf der Naturforscherversammlung in Nauheim 1920 gehaltenen Vortrag. *Arch. Ohr.-, Nas.-, u. KehlkHeilk.*, 1921, *108*: 71–106. [Ch]

984. Thost, [ ]. Die Caisson-Erkrankungen beim Hamburger Elbtunnelbau. *Berl. klin. Wschr.*, 1921, *58*: 1014. [P, Ch]

985. Thost, A. Verletzungen des Ohres durch Luftdruckschwankungen. *Handb. Neurol. Ohres.*, 1928, *2*(1): 429–448. [P, R, Ch]

986. Tomka, [ ]. Ueber Ohrerkrankung bei Caissonarbeitern. Abstr: *Arch. Ohr.-, Nas.-, u KehlkHeilk.*, 1900 *50:* 154. [P, Ch]

B. OTOLOGICAL ASPECTS OF COMPRESSION

As indicated previously, almost all observers who have investigated the medical aspects of compressed air work have been aware of disturbances in the ears during the period of "locking in." One of the early experimental approaches to the problem was that carried out by Magnus (*990*) 1864 who investigated the effects of increasing atmospheric pressure on five subjects. In one individual, there was complaint of ear pains when the pressure reached 1.3 atmospheres (absolute). The ear drums were transparent and tender. One experienced caisson worker felt no pain in the ears until a level of 3.5 atmospheres (absolute) had been attained. In all cases where there was complaint of ear pain, the ear drums were found to be inflamed. Magnus reported that retraction of the drum persisted as long as the pain lasted. Even experienced caisson workers often complained of a roaring in the ears, pain and partial deafness, and, in a large proportion of these individuals, no visible injuries could be demonstrated.

For further consideration of the effects of rising pressure upon the middle ear, the reader should refer to several articles in the previous section and reports by Kusaka and Imasawa (*989*) 1907, Erath (*988*) 1918, and Scott (*992*) 1919.

In 1940, Requarth and Benson (*991*) published a review of observations on 70 cases of tubal blockage. In 64 of these, or 91 percent, there was a definite history or clinical evidence of upper respiratory infection. Within this group of 64, 53 of the patients suffered from the common cold, 4 had sinusitis, and 7 were afflicted with pharyngitis. In the remaining 6 cases, no history or clinical evidence of any infection could be found.

Almour (*987*) in 1942 reported on "blocked ear" of caisson workers. Regarding hearing loss in such cases, he considered that there was no definite characteristic pattern of the disturbance in auditory acuity. Out of 74 cases of "blocked ear," 46 patients suffered from hearing loss in which the question of compensation was an issue. In 19 of these, loss of auditory acuity was greatest for sounds in the 2,048, 4,096, and 8,192 frequencies. In 21 cases, the cause of the defect in hearing lay in the 128, 256, and 512 frequency ranges. In those cases in which no perforation of the drum occurred, hearing usually returned to normal limits within 4 to 28 days as patency of the Eustachian tube was established. In those patients suffering from perforation of the drum, the initial hearing loss was often very slight and affected only the upper tone range (from 1,024 to 8,192). In evaluating the severity of the disability, the injury itself, according to Almour, is not of primary importance but rather the length of time the patient has been working in compressed air. Almour commented upon the difficulty of obtaining accurate statistics on the incidence and severity of deafness in compressed air workers and pointed out that it was not yet possible to decide on compensation on the basis of percentage of hearing loss due to a blocked ear. Adequate standards, the author considered, should be established. He urged the importance of making a survey

of auditory acuity in compressed air workers and recommended that measures should be adopted which would make mandatory an accurate estimation of hearing in such workers before their employment.

987. Almour, R. The "blocked ear" of the caisson worker. *Laryngoscope, St Louis*, 1942, *52*: 75–81. [P]

988. Erath, J. Les épreuves de Valsalva et de Toynbee comme moyen de traitement des troubles auriculaires dûs aux changements brusques d'altitude. *Rev. Laryng., Paris*, 1918, *39*: 476–478.

989. Kusaka, S. and M. Imasawa. (On the congestion of membrana tympani from diving.) *Sei-i-Kwai med. J.*, 1907, *30*(8).

990. Magnus, A. Beobachtungen über das Verhalten des Gehörorgans in komprimirter Luft. *Arch. Ohr.-, Nas.-, u. KehlkHeilk.*, 1864, *1*: 269–283. [P]

991. Requarth, W. H. and R. E. Benson. Compressed air illness with special reference to the middle ear. *Industr. Med.*, 1940, *9*: 115–121. [R]

992. Scott, S. Vertigo and nystagmus associated with inflation of the Eustachian tube. *J. Laryng.*, 1919, *34*: 51–52.

C. AEROTITIS MEDIA AND SINUSITIS

For an early account of otitis media, any of several textbooks on the ear may be consulted; for example, that of Sexton (*1010*) 1888. In 1900, Stephens (*1013*) in his report on accidents and diseases caused by diving operations referred to pain in the ears on descent and called attention to cases of supurative otitis media. In all of these cases, there had been a previous history of "running ears." Otitis media in caisson workers was also discussed in 1908 by Berruyer (*998*) and a case of otitis reported by Beck (*995*) 1919 may also be of interest.

Ear problems in caisson workers were considered in a report by Hughson, Crowe, and Howe (*1007*) published in 1934. The papers of Kennedy (*1008*) 1943 and MacKenzie (*1009*) 1943 may also be consulted. Behnke (*996*) in 1944 stated that the rate of accommodation to increasing pressure in experienced divers is as rapid as 45 lb. per sq. in. per minute. The average time of descent to 225 ft. by student divers in 400 dives was 5.2 minutes (2 to 14 minutes). In helium-oxygen dives, the average descent time for a depth of 225 ft. in 400 dives was 4.6 minutes (2 to 15 minutes). For deep sea dives by experienced divers, the average time was about 3.5 minutes to depths of 225 to 240 ft. (an average of 1.5 to 3.7 minutes per hundred feet). These figures do not represent maximum rates but rather rates well tolerated by healthy subjects and which do not produce trauma of the sinus and aural membranes. Behnke considered the pressure chamber useful as a means of diagnosis of sinus and aural blockage and believed that those who can accommodate a pressure rise at a rate of 45 lb. per sq. in. per minute may be considered free of nasopharyngeal infection. The therapeutic use of the pressure chamber was also referred to.

Aerosinusitis, including its cause, clinical course, and treatment, was discussed by Campbell (*1000*) in 1944. Reference may be made also to an article by Dickson, McGibbon, and Campbell (*1002*) 1944.

In 1944, Teed (*1014*) discussed the factors producing obstruction of the Eustachian tube in submarine personnel undergoing escape training. In training submarine personnel in the use of the submarine escape "lung," each subject is exposed to a pressure of 51 lb. per sq. in. as a preliminary test. Two escapes are made from a diving bell at 12 ft. and then 2 from the 18-foot lock of the training tank. Two escapes from the 50-foot lock and 2 from the 100-foot lock are considered optional but in practice, personnel do not decline to make these escapes. The most common difficulty is that of equalizing the pressure in the ears on "locking in" because of obstruction of the Eustachian tubes. Pain in the sinus areas and tooth pain are also encountered. The author records that between the first of October, 1941 and the first of October, 1942, 5,110 men were given routine tank tests. Of these, 271 were classified as failures on the first trial because of inability to ventilate the ears spontaneously. Of this number, 147 were passed on the second or third attempts; the remaining 124, or 2.4 percent, were disqualified permanently. An apparently statistically significant difference between the number of failures during the May to October period and the October to May period indicated that weather might play some

role. It was considered that the number of failures might be related to the number of upper respiratory infections during the cold season. Seven hundred and eight trainees were examined otoscopically immediately after the tests. A temporary hearing loss was noted in all cases, and in a few, a permanent loss. This loss of auditory acuity was believed to be of the conduction type but in some patients of this series, it was of the higher frequency, perception type. Tinnitus was a symptom in some cases. In addition to evidences of pathological changes in the middle and internal ears, there was also damage to the external canal, consisting of congestion of the skin, especially at the fundus, or hemorrhage into the lumen or subcutaneous hematomata. Sometimes, hemorrhagic blebs were seen on the drum which appeared to be due to dissection of layers of the membrane by extravasated blood. In a few cases, these blebs ruptured and provided a source of bleeding within the external auditory canal. An evaluation of the etiological factors was carried out in some detail. The men who complained of ear pain were found to have less than half the percentage of grade 3 and grade 4 ears than those who endured the pain and said nothing. Statistically, pain was found to bear a reliable relationship to ear damage but from a practical point of view, Teed considered that failure to admit pain in certain personnel made it a very inadequate criterion of ear damage in individual cases. Evidence was presented to indicate that of the commonly stated causes of Eustachian tube obstruction, only upper respiratory infection and possibly allergy were of importance. The growth of lymphoid tissue in the pharynx appears to be a significant factor though this, in turn, may be influenced by other factors. It was considered that irradiation by radium or X-ray was correct therapy in such cases and Teed stated that a limited clinical experience available at that time appeared to support this hypothesis.

Shilling (*1011*) 1944 reported that 30 percent of men undergoing submarine escape training at the U. S. Submarine Base, New London, Conn. had difficulty leading to aerotitis media and hearing loss. Ears showing severe damage were found to have flattened Eustachian orifices and it was suggested that irradiation therapy would be of benefit. Under conditions of careful selection and correct administration of pressure, severe aural pathology and hearing loss need not be as common as it has been. It was considered that repeated trauma to the ears resulting from pressure may result in permanent loss of auditory acuity.

In recent years, considerable attention has been given the prevention and treatment of aerotitis media and allied conditions. For further reports on the radium technique, the reader should refer to page 242. For a consideration of the alleviation and prevention of aerotitis media and tubal and sinus block in compressed air workers by the inhalation of helium-oxygen mixtures, reference may be made to the section on helium administration (p. 290). Reports by the following authors in particular should be referred to: Lovelace, Mayo, and Boothby (*2541*) 1939; Crosson, Jones, and Sayers (*2539*) 1940; Hall (*2540*) 1940; Requarth (*2542*) 1941; Thorne (*2544*) 1943; and Singstad (*2543*) 1944.

In recent studies on aerotitis media, Haines and Harris (*Ann. Otol., etc., St Louis*, in press) followed Teed (*1014*) 1944 in describing and grading the symptomatology of the condition. A perfectly normal ear was described as No. 0. An ear showing some congestion in Shrapnell's membrane and along the handle of the malleus was described as No. 1. Retraction and an extensive and fiery red congestion of the entire drum characterized a No. 2 ear. A No. 3 ear exhibits the same symptoms as No. 2 but, in addition, there is evidence of ruptured vessels in the drum. A No. 4 ear is characterized by extensive vascular rupture, with bleeding in the middle ear and from the Eustachian tube. There may be dissecting hemorrhages in the layers of the ear drum. The ear drum may actually be ruptured or there may be bleb formation in the canal. The whole middle ear may become filled with blood mixed with air, or filled with blood alone, in which case the drum appears purple or black. These last cases have been termed No. 5 ears because of a differential effect on acuity.

An experiment was performed by Haines and Harris in an attempt to discover the causes and effects of aerotitis media and to find the best means of prediction, prevention, and treatment. In the course of this experiment, 6,149 candidates were subjected to 50 lb. pressure in a dry recompression chamber. All subjects (not only those complaining of pain) were examined minutely both before and after pressure by means of the otoscope, the nasopharyngoscope, and the pure tone audiometer. All pertinent data was recorded. A large group of men not contracting aerotitis media in the pressure chamber was required to undergo a second pressure test. Another group which did contract aerotitis media was likewise required to undergo a second pressure test after their otopathology had subsided; this group received no treatment whatever. These two groups served as controls for 5 experimental groups given different types of treatment as follows: psychological, topical, X-ray, radium, and dental. The types of treatment were all based on some rationale designed to assist the men in successfully taking pressure in the future. Psychological treatment included additional motivation and encouragement, the use of chewing gum, and the use of music. None of these things reduced the incidence of aerotitis media on subsequent pressure tests. Topical treatment consisted of one-fourth percent neosynephrine in normal saline, applied locally for several hours before pressure. No effect was noted. X-ray therapy was discontinued for administrative reasons and the results are inconclusive.

Radium therapy consisted in the application of a monel metal cylinder 2 cm. long, outside diameter 2.3 mm., with walls 0.3 mm. thick, containing 50 mg. of radium salt, to the pharyngeal orifice of the Eustachian tube for 8 to 10 minutes. This dose is effective, after 3 to 8 treatments separated by a month, in reducing excessive hyperplastic lymphoid tissue around the opening of the tube, thus permitting many men formerly unable voluntarily to open the tube now to do so. A total of 732 cases of aerotitis media were treated. Well over 90 percent became able to sustain pressure without contracting aerotitis media.

Dental therapy was investigated in several scores of cases where improper jaw motion was suspected of hindering normal operation of the Eustachian tube. Very good success in these cases was achieved.

No very efficient method was found to predict whether a man would contract aerotitis media. Positive correlations were obtained with appearance of Eustachian tubès, whether open, flat, closed, or covered, and with size of adenoids; but the magnitude of the relationship did not permit of good prediction in individual cases. The Valsalva maneuver was indicative only if the individual was very poor in that ability. It was found that pain is not a good indicator either of grade of damage to the ear or of the loss of auditory acuity. Eight percent of men failed the first trial because of pain, while 26 percent of men developed aerotitis media.

Rupturing the ear drum was found to produce a loss in acuity of 5 to 10 decibels. Almost no effect on acuity could be found as a result of aërotitis media unless the middle ear was filled with free blood.

993. Armstrong, H. G. and J. W. Heim. The effect of flight on the middle ear. *J. Amer. med. Ass.*, 1937, *109*: 417–421.

994. Barnes, H. A. Aero-salpingotympanitis with delayed vestibular symptoms. Report of a case. *Nav. med. Bull., Wash.*, 1945, *44*: 830–832. [Ch]

995. Beck, O. Otitis nach Sprung ins Wasser, Sinusthrombose, Inselbildung der Jugularis interna. *Mschr. Ohrenheilk.*, 1919, *53*: 39–40.

996. Behnke, A. R. Physiologic effect of pressure changes with reference to otolaryngolcgy. *Trans. Amer. Acad. Ophthal. Oto-laryng.*, 1944, *49*: 63–71. [P, M]

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D. OTOLOGICAL EFFECTS OF DECOMPRESSION

In 1894, Curnow (*1021*) reported a case of a compressed air worker in the Blackwall Tunnel in London with Ménière's symptoms, including unilateral deafness.

A patient reported by Alt (*1018*) 1896 felt general exhaustion and abdominal pain 1 hour after leaving the caisson. Within a few minutes, there was dizziness and complete deafness. On examination, the tympanic membranes were concave and thickened and the patient was completely deaf in the left ear and partially so in the right ear. He was unable to walk or stand alone and complained of tinnitus in both ears. Considerable improvement was noticed after 16 days. In another case, the patient suffered severe pain in the chest and abdomen as well as shortness of breath soon after leaving the caisson. Within 35 minutes, he was in a state of almost complete collapse but not unconscious. This condition lasted 2 to 3 hours. When seen at the clinic, he complained of intolerable pain in the ears and in the extremities. The tympanic membranes were retracted and livid. The next day he was able to stand, but his balance was seriously impaired. Hearing was markedly reduced on both sides. After 1 month, hearing was still impaired but balance was greatly improved. A third patient left the caisson in apparently good health but was found one-half hour later unconscious and cyanotic. On recovering consciousness, he complained of vertigo and increasing pain in the ears and in the limbs. The tympanic membranes were retracted and hyperemic. After 8 days, there was great improvement in the vestibular function and hearing in the right ear was normal. In the left ear, the patient was completely deaf.

Thost (*1024*) 1911 reported a patient who was stricken with pains in the ear, dizziness, and weakness on emerging from the caisson. He recovered sufficiently to return to work, but 5 months later he suffered another attack with the same symptoms. Three months later, he sought medical advice because of deafness in both ears and dizziness. There was at this time very marked nystagmus and some impairment of mental function. Therapy proved of no avail and 5 months later he was still deaf and showed signs of mental impairment.

Inner ear invo'vement resulting from too rapid decompression was discussed by von Gordon (*1023*) 1926–27 who considered that the etiological factor is bubble formation within the minute blood vessels of the labyrinth. This report contains essentially the same material as that discussed by Alt (*961*) 1897.

A caisson worker reported by Bertoin (*1019*) 1934 was seized with a violent attack of vertigo 1 hour after leaving a caisson during the construction of the Quarantine Bridge, Lyons, France. He fell to the ground and was taken to his home where he remained for 32 days. During this time, he was deaf in the right ear and was troubled by persistent and violent buzzing in the ear. He also complained of attacks of vertigo, especially in the morning, on stooping, or rising, or turning his head rapidly. He was troubled by a sense of uncertainty in his balance but did not actually fall. On examination, both ear drums were gray and tense. The light reflex was absent and there was no scar. The Weber test was localized to the left and the patient was completely deaf in the right ear. On standing on 1 foot and on walking with the eyes closed, he tended to incline to the right. There was no vertigo or nystagmus on injecting 20 cc. or 100 cc. of cold water into the right ear.

The patient had had a similar accident about 2½ months previously. He was seen 4 years later. During this time, he had not been able to return to compressed air work. He still suffered from attacks of vertigo and there were still persistent deafness and noises in the right ear. Examination indicated the same status as 4 years previously, namely, loss of auditory and vestibular function on the right side.

Another patient, aged 48, became dizzy and fell to the ground 15 minutes after leaving the same caisson as the patient described above. For some hours, he had a sense of faulty equilibrium but he apparently recovered sufficiently to take up his work again. About a month later he suffered a similar attack, but this time deafness in the right ear and vertigo persisted. Upon examination, 7 months later, there were unilateral deafness, head noises, and vertigo, especially in the morning. It appeared to the patient that objects rotated around him and he was unable to get up and down a ladder. The right tympanum was retracted and only slightly mobile and he was totally deaf in the right ear. The Weber test was lateralized to the left and he rocked when standing on 1 foot with the eyes closed. The caloric test, carried out with 20 cc. and with 100 cc. of cold water, indicated no reaction in the left ear. Three and one-half years later he was still deaf in the right ear, ear noises persisted, and the attacks of vertigo had become worse.

A compressed air worker, 29 years cf age, had a sense of an explosive noise in the left ear a few minutes after leaving the caisson. He had severe vertigo and fell to the ground. The patient was unconscious for several minutes and when he came to, he was deaf in the left ear and there was some loss of hearing in the right ear. He remained in bed for 15 days with vertigo. After this he felt better but was unable to do any work. When seen 6 months later, he was deaf in the left ear and complained of incessant ear noises on the same side. He suffered frequent attacks of vertigo, especially on effort or on getting up. He had a sense of objects rotating about him and would fall to the left side. He had fallen many times and his face was covered with the scars of injuries received in this way. Upon examination, he was totally deaf in the left ear, and on standing on 1 foot with the eyes closed, he fell to the left and backwards. The caloric test showed no reaction in the left ear. He had hemianesthesia of the left side of the face. In this case, there was total destruction of the left labyrinth with a partial lesion of the right labyrinth as well as an involvement of the left trigiminal nerve. It appears that the damage was irreversible and that no improvement could be expected.

Bertoin (*1019*) 1934, in commenting on these cases, emphasized that labyrinthine lesions are rarely seen as an accident of decompression. For example, out of 53 cases of ear disturbances reported by Berruyer (*967*) 1908, only 2 appeared to be of labyrinthine origin. Bertoin believed that these ear lesions were caused by gas bubbles which obstructed small blood vessels in the inner ear. A rise of blood pressure on leaving the caisson was also considered a possible cause of the inner ear disturbance. In either case, it was believed that hemorrhage or exudation might occur.

The following typical picture of inner ear disturbance due to decompression was given by Bertoin: Characteristically, the victim was

attacked within about 15 minutes to 1 hour after leaving the caisson. He has a severe attack of vertigo and falls to the ground. He may lose consciousness and when he comes to, complains of loss of hearing usually complete on one side and often partial on the other. There are violent noises in the affected ear and he is forced to take to his bed because of the attacks of vertigo. In bed, he feels better and the condition may gradually improve. Deafness usually persists and vertigo is complained of on stooping, arising, or rapidly turning the head. There is tinnitus and a sensation of external objects turning. The affected labyrinth is unexcitable. These cases correspond to Lestienne's (*1404*) 1933 third category in which the lesion is persistent and total, and probably due to hemorrhage within the inner ear. Bertoin stressed the importance of examining the labyrinth in assessing prognosis.

In 1938, Bertoin (*1020*) published a further report on labyrinthine disturbances caused by decompression. A caisson worker of 48 years of age, after working at a depth of 20 m. began to have malaise and vertigo while still in the decompression chamber. He succeeded in getting home, but even in bed external objects appeared to rotate. He complained of intolerable headache and intense noises in the ears. One and one-half months later, he still had vertigo on bending and some hearing difficulty in both ears. Upon examination, both ear drums appeared normal and there was approximately a 25 to 30 percent diminution in auditory acuity on each side. Labyrinthine reactions were normal.

A 24-year-old caisson worker felt unwell some minutes after leaving the caisson and went home. After lunch, he had a sensation as if he had been shot on the right side and fell to the ground. He spent 12 days in bed during which time he had vertigo whenever he turned his head. He resumed work in the caisson a little over a month after the original accident but because of attacks was forced to abandon work under pressure and took a job on the outside. As the vertigo diminished, his auditory acuity gradually decreased and when seen 10 months after the accident, there was practically complete deafness in the right ear.

1018. Alt, F. Ueber apoplectiforme Labyrintherkrankungen bei Caissonarbeitern. *Mschr. Ohrenheilk*, 1896, *30*: 341–349. [P, Ch]

1019. Bertoin, R. Pronostic éloigné des accidents labyrinthiques par décompression. *Ann. Oto-laryng.*, 1934, *1*: 407–411. [Ch]

1020. Bertoin, R. A propos des accidents labyrinthiques par décompression. *J. Méd. Lyon*, 1938, *19*: 457–460. [With Esperanto summary.] [Ch]

1021. Curnow, J. Auditory vertigo caused by working in compressed air. *Lancet*, 1894, *2*: 1088–1089.

1022. Gandino, D. La malattia dei cassoni dal punto di vista otoiatrico. *Rass. Med. Lav. industr.*, 1940, *11*: 142–148. [R]

1023. Gordon, L. von. Die Berufskrankheiten des Gehörorgans. *Zbl. Hals-, Nas.- u. Ohrenheilk.*, 1926–27, *9*: 433–461. [R]

1024. Thost, [ ]. Caissonkrankheit. *Dtsch. med. Wschr.*, 1911, *37*: 1101. [Ch]

E. HEARING IN COMPRESSED AIR WORKERS AND SUBMARINE PERSONNEL

In the early literature on the subject, mostly from studies on caisson workers, the question of the etiology of deafness is complicated by several factors. In the first place, only relatively crude tests of hearing could be administered. In the second place, the reason for deafness could usually not be determined; it could have been caused (a) by the immediate action of compressed air in telescoping the ossicles, (b) by lesions due to previous attacks of aerotitis media, (c) by nitrogen bubbles in the fluids of the inner ear, or (d) it may have existed prior to the investigations.

In 1898, Lester and Gomez (*1031*) made observations on the effects of compressed air on the hearing of eight subjects in the caisson of the East River bridge construction. Hearing of each subject was tested before entering the caisson and while under a pressure of 3 and 3.5 atmospheres (absolute). Lester and Gomez concluded that both bone conduction and air conduction were considerably reduced while under pressure and that the diminution in auditory acuity is proportional to the rise in atmospheric pressure. It was believed that bone conduction was more seriously interfered with than air conduction. In Lester and Gomez's experiments, the lower tones were stated to be unaffected. Hearing for both whispered and spoken words was greatly de-

creased while in the caisson and certain vowels and consonants could not be heard at all. On this point, there was individual variation. These effects on auditory acuity persisted for 24 to 48 hours after leaving the caisson.

Poli (*1034*) in 1909 carried out examinations on 205 experienced caisson workers and 168 inexperienced applicants for caisson work. Fourteen and six-tenths percent of the former and 7.6 percent of the latter were refused employment because of diminished hearing. A total of 30 individuals (22 experienced caisson workers and 8 inexperienced applicants) were refused because of noises in the ears and dizziness. Only 3 percent of the workers accepted at the end of the examination suffered subsequent ear disturbances as compared to approximately 10 percent of unselected workers employed on the bridge construction at Nussdorf.

For other studies dealing with hearing loss as a result of compressed air, the reader may consult (a) the paper by Poli published in 1909 on prophylactic examination of hearing in compressed air workers, (b) the report of Bijlsma (*1026*) 1901–2 on diver's deafness, (c) the report by Kos (*1030*) published in 1944 on the effect of high altitude on hearing, and (d) a report by Machle (*1033*) 1944 on the effect of gun blast upon hearing. Other papers related to the subject are those of Politzer (*1036*) 1868, Cordes (*1029*) 1900, and von Békésy (*1025*) 1929.

A most valuable paper on auditory acuity in submarine personnel is that published in 1942 by Shilling and Everley (*1037*). This report is a résumé of some 1,500 otological examinations of submarine personnel. With regard to hearing loss due to Diesel engine noise, Shilling and Everley stated that the major loss occurred in the first hour of exposure with slight increase for 2-, 3-, and 4-hour exposures. After an exposure of 1 hour, 5 hours were required for recovery of normal auditory acuity while after 4 hours' exposure, recovery often required as long as 20 hours. Permanent hearing loss at the 2,048 to 8,192 frequency levels was found, and such permanent loss of hearing became more frequent with increasing length of service. There was evidence of damage of the cochlear mechanism and nerve degeneration as well. Personnel engaged in radio work under severe conditions also suffered hearing loss depending upon duration of exposure. The hearing loss in these cases was noticeable at both the low and high frequencies though there was a greater loss for the higher frequencies. Radio duty aboard submarines was not a necessary condition to a loss in auditory acuity since many radiomen without submarine duty also showed hearing loss. Trauma and similar factors were eliminated in this study. It was suggested that in these cases the hearing loss may have resulted from some repeated acoustic insult such as "blasting" in the radio. The authors suggested that all radio equipment should be so constructed as to eliminate the possibility of such acoustic shocks. The study also proved that a "normal" audiogram is not necessarily a prerequisite for excellence as a radio or "sound" operator.

In part III of Shilling and Everley's report a discussion is given of aerotitis media in submarine escape training. It was pointed out that 152 out of 866 men had to request discontinuance of the pressure test because of blocking of the ears, usually before 10 lb. pressure was reached. One hundred and thirty-nine men had to have the pressure rise discontinued once or twice during the test. A review is given of earlier work on aerotitis media and the treatment of the condition by Eustachian tube catheterization, warm oil in the ear, ephedrine, and inhalation of helium-oxygen mixtures. Hearing loss due to exposure to increased air pressure is also summarized. Shilling and Everley stated that acute hearing loss due to unequalized pressure usually returns to normal within a few days and that the degree of damage as determined by otoscopic examination is not consistent with audiometer tests. It has also been found that the loss of hearing may increase on the second or third day before improvement is noted. Permanent hearing loss was usually found to be in the higher frequency ranges when due to exposure to increased air pressure. In caisson workers, hearing loss is usually proportioned to total time of exposure to compressed air, while deep sea divers, as a whole, tend to show

no loss of acuity in spite of exposure to compressed air.

Part IV of Shilling and Everley's article should be consulted for a consideration of hearing loss due to exposure to gun fire. Both temporary and permanent deafness among men exposed to heavy gun fire have been reported and permanent loss appears to be most marked in the high frequencies, particularly at 4,096 and 8,192. In some cases, "hyperesthesia acoustica" has been noted in which the patients experience pain and discomfort when subjected to loud noises. According to one point of view, hearing loss resulting from explosions is due, not to trauma in the middle ear, but to damage to nerve structure in the cochlea. Shilling and Everley discussed various protective measures.

1025. Békésy, G. von. Zue Theorie des Hörens. *Phys. Z.*, 1929, *30:* 115–125.

1026. Bijlsma, R. Duiker-doofheid. *Med. Weekbl.*, 1901–02, *8*: 273–275.

1027. Campbell, P. A. The problem of aviation deafness; the airman, his history and his plane. *Arch. Otolaryng., Chicago*, 1945, *41:* 319–321.

1028. Campbell, P. A. and J. Hargreaves. Aviation deafness, acute and chronic. *Arch. Otolaryng., Chicago*, 1940, *32*: 417–428.

1029. Cordes, H. Apparat zur Luftverdünnung im äusseren Gehörgange mit manometrischer Bestimmung des negativen Luftdruckes. *Ill. Mschr. ärztl. Polyt.*, 1900, *22*: 169–170.

1030. Kos, C. M. Effect of barometric pressure changes on hearing. *Trans. Amer. Acad. Ophthal. Otolaryng.*, 1944, *49*: 75–81. [P, M]

1031. Lester, J. C. and V. Gomez. Observations made in the caisson of the new East River bridge as to the effects of compressed air upon the human ear. *Arch. Otol., N. Y.*, 1898, *27*: 1–19. [P]

1032. McGibbon, J. E. G. Aviation pressure deafness. *J. Laryng.*, 1942, *57*: 14–22.

1033. Machle, W. The effect of gun blast upon hearing. *Trans. Amer. Acad. Ophthal. Oto-laryng.*, 1944, *49*: 90–96. [M]

1034. Poli, [ ]. Ergebnisse der Untersuchung des Gehörapparates bei Caissonarbeitern vor der Aufnahme zur Arbeit. *Mschr. Ohrenheilk.*, 1909, *43*: 313. [P]

1035. Poli, C. Risultati dell'esame preventivo dell'orecchio nei lavoranti in aria compressa. *Policlinico*, Sez. pract., 1909, *16*: 210–211. [P]

1036. Politzer, A. Ueber die günstigen Resultate der durch Luftdruck erzeugten Rupturen dünner Trommelfellnarben. *Wien. med. Pr.*, 1868, *9*: 6–8; 39–40; 93–95; 116–118.

1037. Shilling, C. W. and I. A. Everley. Auditory acuity among submarine personnel. *Nav. med. Bull., Wash.*, 1942, *40*: 27–42; 396–403; 664–686; 938–947. [P, M]

1038. Shilling, C. W., I. A. Everley, and J. D. Harris. Hearing tests: an evaluation. *Nav. med. Bull., Wash.*, 1945, *44*: 100–116.

III. DECOMPRESSION SICKNESS

A. GENERAL STUDIES

A number of monographs and reports of general interest on the subject of decompression sickness may be consulted.

The term "decompression sickness" is used in this Sourcebook to include the signs, symptoms, and underlying pathology arising from rapid reduction of barometric pressure in caisson and tunneling operations or in diving. The term also covers the harmful effects of decompression to levels of less than 1 atmosphere as experienced in high altitude flights or in experimental decompression chambers. Use of the term "decompression sickness" recognizes that the effects of decompression on the body are basically the same at all pressure ranges. Decompression from pressures above 1 atmosphere may cause more profound symptoms than decompression to levels below 1 atmosphere but the etiological factor is the same in both cases. In this Sourcebook, such terms as "caisson disease," "diver's paralysis," "diver's itch," "bends," "chokes," etc., are used to denote special conditions of occurrence or specific manifestations of decompression sickness. In describing a particular investigator's work, his own terminology for the condition is often followed. Where an inclusive term is required, "decompression sickness" is preferred usage.

Although earlier allusions to the effects of compressed air in caisson work have been published, a thesis by Bucquoy (*1055*), which appeared in 1861, constitutes one of the earliest reports in which the subject has been adequately summarized. This thesis includes a history of the development of the caisson, a description of the effects of "locking in," and the physiological effects of raised atmospheric pressures. Pathological changes resulting from exposure to such conditions are described and

the gas bubble theory of caisson disease, originally proposed by Hoppe (*1329*) 1857 is referred to. Bucquoy called attention to the prevention of caisson disease by slow decompression.

Reference should also be made to a volume published in 1896 by Snell (*1148*) on compressed air illness. This work covers the history of the subject and includes the diagnosis, etiology, morbid anatomy, and treatment of caisson disease. A number of case histories are reported. Case histories may also be found in a thesis submitted in 1901 by Houdeville (*1086*). This report includes accurate descriptions of the symptoms, diagnosis, prognosis, and treatment of caisson disease. An excellent review of the subject is also to be found in an article by Kabhrel (*1088*) 1903.

An investigation of the literature in this field would not be complete without a study of the comprehensive monograph on decompression sickness published in 1900 by Heller, Mager, and von Schrötter (*28*).

An English report on caisson disease which very completely covers the problem of compressed air illness is a long article by Parkin (*1129*) 1905. The reader will find in this paper a review of early diving operations, a description of case histories, and physiological observations made in connection with the building of the foundations of the Tyne River Bridge. Symptoms of caisson disease are described in detail and Parkin also gives a critical analysis of the then current theories of the etiology of the disease. It is of interest that Parkin attributes the formulation of the air embolism theory to Rameaux in 1861. This theory, according to Parkin, explains a large number of the symptoms encountered. An outline is given of the prevention of caisson disease by slow decompression. The author believed that too much emphasis had been placed on purity of air and ventilation in preventing caisson disease. Pressure was the main factor and the condition could be prevented only by attention to decompression rates.

British experience with caisson disease in connection with bridge building was also summarized in two papers by Oliver (*1121*, *1122*) 1905 and 1905–6. Oliver stressed the need for an abundance of pure air in the caisson and emphasized the importance of careful selection of personnel. Frequent checks on the health of workers by a medical officer should be carried out. Oliver's experience with caisson disease was gained at Newcastle-on-Tyne during the construction of bridges across the Tyne. His later paper (*1122*) 1905–6 contains a review of the symptoms of caisson disease, its physiology and pathology, and methods of prevention and treatment. It was recommended that recompression be carried out as quickly as possible as an essential method of treatment.

In addition to the long monograph by Heller, Mager, and von Schrötter (*28*), the reader should refer to a thesis by Heller (*1080*) which appeared in 1912. This monograph summarizes views on prevention and treatment of the condition and describes the organization of the medical service for the protection of caisson workers.

One of the outstanding investigators in the field of caisson disease and the physiology of work in compressed air in England was Leonard Hill. Much of his work is summarized in a volume published by him in 1912 (*1083*).

Keays (*1089*) 1912 published a report on 3,692 cases of compressed air illness in the building of the East River Tunnel in New York. This paper briefly reviews questions of the etiology of caisson disease as well as symptoms, pathology, treatment, and prevention of the condition. Keays stated that while much may be done by appropriate regulations to reduce the number of cases of illness and death in compressed air work, nevertheless, when pressures of 2 or more atmospheres are being used, it should be classed as a dangerous occupation.

A very complete review of the general subject of caisson disease is to be found in an article by Erdman (*1067*) 1916. This paper is comparatively short but contains a large amount of information and is, therefore, particularly useful to the reader desiring to gain a familiarity with the subject of caisson disease in a relatively brief time. Erdman covered the history of work under compressed air and gave figures on the frequency of occur-

rence of caisson disease in various important bridge construction and tunneling operations. He also discussed in some detail theories of the etiology of caisson disease and considered the various predisposing factors, including (a) atmospheric conditions above ground; (b) degree of pressure; (c) length of exposure; (d) noxious gases in the working environment; and (e) various individual factors such as age, obesity, cardiovascular efficiency, alcoholism, fatigue, cold, and organic disease. The symptoms of caisson disease were described in detail in order of frequency and the reader will find a classification of the symptomatology which may be useful. Chronic effects of work in compressed air are given and the mortality figures are also discussed. Regarding treatment, Erdman gives tables setting forth hours of work at various pressures as promulgated in various regulations. Erdman's discussion of treatment and prevention of caisson disease is summarized in more detail on page 269 of this Sourcebook.

For a further general study on caisson disease, Erdman's article (*1068*) published in 1924 may be consulted. This paper is particularly useful for its description of the history of the caisson and of caisson disease. A more recent general review by Wright and Brady (*1162*) 1929 also merits attention. Figures are given from various sources on the incidence of decompression sickness and its mortality. Symptoms are described as well as postmortem findings in experimental animals and workers dying of caisson disease. Wright and Brady discussed the predisposing factors in caisson disease. The paper also contains references to ventilation of caissons, selection of workers, and decompression and recompression procedures. Singstad's long article (*39*) on industrial operations in compressed air, published in 1936, has been frequently referred to and should be consulted for a very complete consideration of the whole subject of decompression sickness. Similarly, a brief article by Schmidt (*1138*) 1938 is useful. For modern authoritative treatments of the subject of caisson disease, the publications of Behnke and Shilling must be carefully studied. Attention is called to a report in 1943 by Behnke (*1048*) on the military environment in relation to changes in barometric pressure as applied to clinical medicine. For further reports by Behnke, the reader should consult the Index (p. 359).

Two of the most complete studies on caisson disease are those published by Shilling (*1141*, *1142*) in the Naval Medical Bulletin in 1938 and 1941. The reader should become thoroughly familiar with the contents of these carefully prepared articles. They contain classified bibliographies and a detailed analysis of the literature on caisson disease. The first article (*1141*) is particularly useful for its description of the theories which have been proposed and advocated to explain the etiology of caisson disease. Shilling's classification of the symptoms of caisson disease has been used in outlining the clinical picture of decompression sickness in the following sections. Shilling described the symptomatology in great detail and also gave a discussion of the diagnosis and pathology of the condition. The report also contains an authoritative discussion of methods of treatment and prevention. The later article (*1142*), published in 1941, brings the subject up to date.

Attention should be called to a long monograph by Smith (*76*) published in 1873 on the effects of high atmospheric pressure including caisson disease and an article by Van Rensselaer (*1350*) 1891. Reference is made to both of these articles in other places in this Sourcebook but they are referred to again because, in spite of the fact that they are both relatively early reports, they contain a wealth of information and accurate clinical descriptions of the effect of raised atmospheric pressures and decompression on caisson workers. The report by Smith, who first used the name "caisson disease," is based in part upon his experience as medical officer attached to the construction of the Brooklyn Bridge in New York. Van Rensselaer's review is especially useful for a large series of case descriptions of caisson disease, not only those personally seen by Van Rensselaer, but also cases described in the literature by other observers. Summaries of autopsies are also given, as well as cases in which microscopic examination of the spinal

cord was carried out. Van Rensselaer's paper should also be consulted for a detailed review of the theories of the etiology of caisson disease. This analysis is one of the most complete in the literature. It is of particular interest since Van Rensselaer adhered to the congestion theory and argued against the view that caisson disease is caused by the production of air bubbles in the blood and tissues.

A number of reports on the general aspects of decompression sickness with particular emphasis on work in caissons may be consulted. References by the following authors have been selected because of their special bearing on the general problem of decompression sickness in caisson workers: Willemin (*1161*) 1860, Caffe (*1056*) 1863, Barella (*1046*) 1868, Michel (*1110*) 1880, Gérard (*1074*) 1884, Meigs (*1109*) 1885, Smith (*1147*) 1885, Schmitz (*1139*) 1887, Knapp (*1093*) 1891, Friedrich and Tauszk (*1072*, *1073*) 1896, Leffmann (*1105*) 1897, Tomka (*1156*) 1897, Aldrich (*1042*) 1898-99, Oliver (*1118*) 1899, Swiątecki (*1152*) 1899, Biggar (*1051*) 1900, Carré (*1058*) 1902, Aldrich (*1043*) 1900, Giglioli (*1077*) 1902, Picard (*1131*) 1903, Parkin (*1128*) 1903–4, Fournaise and Berruyer (*1070*) 1904, Aldrich (*1044*) 1904, von Mouillard (*1115*) 1904, Waller (*1159*) 1904, Brand (*1054*) 1905, Oliver (*1120*) 1904, Wasserberg (*1160*) 1905, Oliver (*1123*, *1124*) 1906, Carnot (*1057*) 1906, Tooth (*1157*) 1906, Kropveld (*1097*) 1906–7, Constant (*1061*) 1907, Klieneberger (*1092*) 1907, Kropveld (*1098*, *1099*) 1907, Silberstern (*1143*) 1907, Citroen (*1060*) 1908, Haldane (*1078*) 1908, Kropveld (*1100*) 1908, van der Kwast (*1101*) 1908, Verschuijl (*1158*) 1908, von Leliwa (*1106*) 1909, Oliver (*1125*, *1126*) 1909, Peraldi (*1130*) 1910, Silberstern (*1145*) 1909, Bassoe (*1047*) 1911, Heijermans and Kooperberg (*1079*) 1911, Bornstein (*1052*) 1912, Cattaneo (*1059*) 1912, Dominguez (*1063*) 1912, Erdman (*1066*) 1912, Minkowski (*1111*) 1912, Ryan (*1137*) 1912, Silberstern (*1146*) 1912, Frémont (*1071*) 1912-13, Podskrebaeva (*1132*) 1913, Poledne (*1133*) 1913, Holtzmann and Koelsch (*1085*) 1914, Lecaplain (*1104*) 1914, Elizalde (*1064*) 1915, Kober and Hanson (*1094*) 1916, Müller (*1116*) 1918, Moriani (*1114*) 1918, Henderson and Haggard (*1082*) 1923, De Veaux (*1062*) 1930, Oliver (*1127*) 1934, Stott (*1151*) 1934, Bienvenu (*1049*) 1935-36, Langelez (*1102*) 1936, Lipkowič (*1107*) 1936-37, Holstein (*1084*) 1938, Gerbis and Koenig (*1076*) 1939, Gerbis (*1075*) 1939, Henderson (*1081*) 1939, Irby (*1087*) 1939, Koenig (*1095*, *1096*) 1939, Bierman (*1050*) 1943, Stewart (*1149*) 1943, Thorne (*1155*) 1943, Meakins (*1108*) 1944, Moore (*1113*) 1944, and Murphy (*1117*) 1944.

For general studies on compressed air illness with particular reference to tunnelers, attention is called to articles by the following authors: Moir (*1112*) 1896–97, Erdman (*1065*) 1907, Porter (*1134*) 1907, Lauenstein (*1103*) 1909, Roucaÿrol (*1136*) 1911, Branco (*1053*) 1925, Thorne (*1154*) 1941, and Allan (*1045*) 1942.

The clinical picture of decompression sickness in divers is similar to that in caisson workers. However, divers may be subjected to considerably greater pressures than tunnelers or caisson workers. Symptoms are, therefore, sometimes more severe in divers than in other compressed air workers and central nervous system disturbances somewhat more frequent. For general references to decompression sickness applied to divers, articles by the following authors are recommended: Khrabrostin (*1090*) 1888; Oliver (*1119*) 1902; Abbamondi (*1039*, *1040*, *1041*) 1902, 1905, and 1906; Silberstern (*1144*) 1908; Forgue and Jeanbrau (*1069*) 1909; Terni (*1153*) 1911; Stewart (*1150*) 1913; and Rainsford (*1135*) 1942.

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1165. Anon. Caisson disease. *Lancet*, 1905, *1:* 1173. [R]

1166. Anon. Wetsontwerp tot beveiliging der caisson-arbeiders. *Ned. Tijdschr. Geneesk.*, 1905, *41*(1): 857–858; 1078–1800; 1142–1143. [R]

1167. Anon. Will aviators have caisson disease? *Literary Dig.*, 1917, *55*(10): 26. [R]

B. CLINICAL PICTURE OF DECOMPRESSION SICKNESS

1. INTRODUCTION

In addition to the literature reviewed in this section, the reader should also consult the sections on the physiological effects of high atmospheric pressures and the physiological effects of decompression from pressures higher than 1 atmosphere (pp. 23 and 38). The latter section includes studies on nitrogen saturation and desaturation, the physiology of bubble formation, and studies on total body fat in relation to susceptibility to decompression sickness. As defined by present usage, decompression sickness comprehends those signs and symptoms and pathological processes caused by subjecting the body to a fall in atmospheric pressure. The term "decompression sickness" applies to the effects of decompression both from atmospheric pressures greater than 1 atmosphere and from pressures of 1 atmosphere or less from which, thus, tunnelers, divers, and aviators may suffer. Workers in decompression chambers may also show like symptoms.

Caisson disease was defined in 1873 by Smith (*76*) as a disease depending upon increased atmospheric pressure, always developing after removal of the pressure. It is characterized by moderate or extreme pain in one or more of the extremities and sometimes in the trunk and there may or may not be epigastric pain and vomiting. In some cases, the pain is accompanied by a more or less complete paralysis which may be general or local but is most frequently confined to the lower half of the body. Cerebral symptoms such as headache and vertigo are sometimes but less frequently present. The above symptoms are connected, at least in the fatal cases, with congestion of the abdominal viscera and frequently of the brain and spinal cord. This definition as set forth by Smith indicates the extremely wide range of signs and symptoms which may be presented in caisson disease. In attempting a classification of the disease on the basis of signs and symptoms, it is well to remember that although some cases may present only pain, pruritus, or some other isolated complaint, usually the symptomatology is multiple with some feature or features predominating in the clinical picture.

2. CLASSIFICATION ON THE BASIS OF SIGNS AND SYMPTOMS

For a detailed analysis of the literature on compressed air illness, the reader should not fail to refer to Shilling's comprehensive review (*1141*) published in 1938 and two subsequent papers (*1171, 1142*) which appeared in 1940 and 1941. These papers are particularly valuable as bibliographical sources. Shilling classified the symptomatology of caisson disease as it relates to the various body systems, namely: (a) the cerebrospinal system; (b) the cardiovascular system; (c) the pulmonary system; (d) the urogenital system; (e) the structural system (including osseous, connective, muscular, and fatty tissues); and (f) the dermal sys-

tem. The classification used in the present Sourcebook is a modification of Shilling's classification. The literature on the clinical picture of caisson disease will be discussed under the headings given below. Because of the possible multiplicity of symptoms in any one case, it will not be expected that only one feature of the clinical picture will necessarily be manifested. (a) Painful involvement of the structural system, including osseous, connective, muscular, or fatty tissue (the "bends"). (b) Pulmonary involvement. (This includes attacks of dyspnea and feelings of oppression in the chest known as the "chokes." Such symptoms are rarely isolated and are usually grave.) (c) Involvement of the integument. (This includes itching of the skin, formication—known to the French caisson workers as "puces,"—swelling, subcutaneous emphysema and mottling, marbling, and lividity of the skin. In this category may also be included cases of subconjunctival hemorrhage. Skin manifestations may be present without serious symptoms; in fact, caisson workers themselves have in the past believed that those who have the "puces" are usually spared more serious forms of the disease.) (d) Involvement of the autonomic and the central nervous systems. (In such cases, the clinical picture is usually complicated. There may be motor and sensory disturbances, and permanent or transient paraplegias are not uncommon. More rarely, hemiplegia with or without facial paralysis may be encountered and visual disturbances have been reported. In the latter instances, there is loss of visual acuity and there may be contraction of the visual fields, optic neuritis, or optic atrophy. For a further consideration of these somewhat rare visual manifestations, the reader should consult the section on eye lesions (p. 153). Although most of the central nervous symptoms are referable to pathological processes in the spinal cord, nevertheless cerebral symptoms are encountered. These take the form of convulsive seizures, word-blindness, aphasia, neuroses, and psychoses. Associated with disturbances of sensory and motor functions, there may be temporary or permanent loss of bladder and rectal control with retention or incontinence of urine and feces. In some instances, the cause of death may be bladder infection associated with long-continued paralysis of the bladder wall and repeated catheterization. Death may also result from decubitus ulcers. For further studies on the central nervous manifestations of caisson disease, the reader should consult the section on lesions of the central nervous system (p. 145).) (e) Otological disturbances. (There are a number of symptoms associated with compression itself which are not to be included in the definition of caisson disease. These comprehend such manifestations as pain and other symptoms referable to the ears due to difficulty of equalizing the pressure in the middle ear. Aerotitis media or acute otic barotrauma, as it is perhaps more appropriately termed, is a condition from which divers and caisson workers may suffer but it is not, properly speaking, a feature of caisson disease. On the other hand, workers in compressed air occasionally are seized with attacks of vertigo, vomiting, and deafness shortly after return to normal air. These symptoms are ascribed to formation of emboli or to congestion within the labyrinth. Both this condition and ear disturbances associated with compression are discussed in the sections on ear, nose, and throat disturbances (p. 94) and ear lesions (p. 154). (f) Visceral disturbances. (Postmortem examination of acutely fatal cases of caisson disease often yields evidence of bubble formation, congestion, hemorrhage, or other involvement of internal organs such as the liver, spleen, or kidneys. Lesions in these viscera are, however, for the most part "silent" and symptoms definitely referable to these organs are not usually encountered. However, victims occasionally suffer from acute abdominal pain with nausea and vomiting and these attacks, often extremely violent, may be due to gas bubbles in the omental, mesenteric, or gastric vessels.) (g) Sudden death or death in the acute phase of the disease. (Observers have frequently reported how apparently close to death a victim of decompression sickness may be and still recover. However, patients do drop dead within a few minutes of the onset of grave symptoms or die

within a few hours after developing such symptoms. These cases have been attributed to massive air embolism in the coronary or pulmonary vessels or in the chambers of the heart. Conceivably also, some cases of sudden or acute death may be due to some profound pathological process involving the higher levels of the central nervous system.)

3. GENERAL DESCRIPTION OF SIGNS AND SYMPTOMS

Smith (*76*) 1873 described pain as usually the first and most characteristic symptom of caisson disease. According to him, pain was seldom absent. Often the pain is abrupt as if the patient had been struck by a bullet. The suffering may be extreme and Smith likened it to the pain of the flesh being torn from the bones. In his cases, it was usually remittant or paroxysmal and was made worse on attempts at movement. The pain was most usually present in one or both knees, shifting to the legs and thighs and often appeared in the shoulders and arms. Sometimes, the pain was reported in the lumbar area. Tenderness was also associated with the pain, together with painful stiffness of muscles or joints. Swelling and heat were sometimes observed followed later by bruise-like discoloration. Smith reported two cases in which there were minute extravasations of blood in the skin at the seat of pain as if the skin had been spattered with red ink. In one case, there was recurrent swelling of the mammary gland. The skin was generally cool at first and often of a slightly leaden hue. Nearly always, the pain was associated with profuse cold sweat, the perspiration standing out in beads. This was sometimes seen in cases where the pain was not extreme. Acceleration of the pulse depended on the general physical condition. The temperature was usually normal. Smith also differentiated cases of epigastric pain with vomiting which symptoms were present in 24 percent of his cases. The original pressure to which Smith's patients were subjected was never above 35 lb. per sq. in. He notes that gastric symptoms were present in 66 out of 77 cases reported by Jaminet in which workmen were exposed to pressures of 40 lb. per sq. in. and above. Paralysis was seen in about 15 percent of Smith's cases, whereas, out of the 77 cases of workers suffering from caisson disease reported by Jaminet, 47 cases or 61 percent suffered from motor disturbances. Smith observed that the lower extremities were most frequently involved but that the paralysis might also include the trunk or one or both arms. Rarely, the arms alone were affected. Paralysis usually supervened after the onset of pain; disturbances of sensation were seen as well as motor loss. However, pain usually continued. For example, a leg might be entirely insensible to pin-prick and yet be the seat of extreme suffering. This pain and paralysis might exist separately or together.

The degree of motor loss was found to vary from a slight weakness with minimal impairment of sensation including a loss of "hold on the ground" in walking, to complete loss of motion and sensation in the affected part. Even minor degrees of motor deficit of lower extremities were generally associated with some impairment of bladder function. Smith also described cases in which cerebral symptoms predominated. Such patients complained of headache, dizziness, double vision, and incoherence of speech. Manifestations were sometimes followed by unconsciousness and in some patients, there was profound coma.

Moeller (*2185*) in 1881 stated that difficulty was ordinarily experienced by workers on decompression from less than 2 atmospheres. Some workers complained first of the "puces" which developed later to frank pain. There was sometimes painful swelling of those muscles subjected to the hardest work. On decompression from working pressure above 3 atmospheres, grave accidents sometimes occurred in which were observed such symptoms as deafness, disturbances of locomotion and general sensation, especially paralysis of the lower limbs, bladder, and rectum. Moeller also called attention to loss of consciousness, coma, and sudden death. The workers were usually attacked within a few minutes to several hours after leaving the chamber, although symptoms sometimes were delayed over 24 hours.

Oliver, Smith, and Snell (*1189*) in 1904

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observed "bends" mainly in the region of the knees. These pains were attributed by the workmen themselves to the presence of gas in the muscles. It was suggested that such pain might be due to pressure upon small nerve fibers adjacent to capillaries distended by gas bubbles. Oliver and his coworkers also observed cases in which the chief complaints were giddiness, epistaxis, and bleeding from the ears. Cases were seen in which there was loss of power in the legs lasting for hours, days, or months. In several workmen, there was loss of consciousness and some were stricken with blindness. In the Tyne construction operations, two patients showed maniacal symptoms with delusions, delirium, and acute terror associated with great pain in the joints. Abdominal pain and vomiting were also reported as well as sensory loss in the lower limbs. Urinary retention was a relatively common finding and was often associated with numbness, formication in the legs, and loss of anal sphincter control. In these cases, the knee jerks were often exaggerated and ankle clonus was present. Sometimes such patients pursued a chronic course with the development of decubitus ulcers.

Erdman's article on compressed air illness published in 1916 (*1067*) may be consulted for a detailed classification of the symptoms of caisson disease. He reported pain in 88 percent of his cases either as the only symptom or associated with other disturbances. He observed "bends" most frequently in the region of the knees. Next in order of frequency were pains in the elbows and shoulders. Five percent of the cases with pain localized their distress in the abdomen. Erdman observed that abdominal pain was often preceded or accompanied by severe prostration or paralysis. He considered that "bends" could probably be explained on the basis of irritation of peripheral nerves and nerve terminals by bubbles of gas in nerve sheaths, in fascial tissue, beneath the periosteum, or within bone marrow. Numbness, anesthesia, and paresthesias might be similarly explained. Erdman noted that the "puces" was usually never serious and thought it was due to expanding bubbles in sweat glands or possibly due to bubbles in the subcutaneous tissue. "Bends," as well as paresthesias, have from time to time been attributed to irritation of posterior nerve roots by bubbles in the spinal fluid but the best evidence indicates that the etiological factor operates peripherally. Erdman also observed symptoms referable to the higher levels of the central nervous system such as unconsciousness, stupor, collapse, temporary asphasia, and incoherence of speech. There were also such disturbances as convulsions, headache, nystagmus, hemiparesis of the tongue, hemiplegia, and monoplegia. Erdman reported vertigo in over 50 percent of his cases and ascribed this symptom to the formation of bubbles in the labyrinth or the cerebellum. Disturbances referable to the spinal cord, as well as transient blindness and diplopia were reported.

A group of cases was also differentiated in which the symptoms were particularly referable to the cardiovascular system. In some cases brought to autopsy, there were collections of gas in the right heart and the bluish mottling on the chest or abdomen noted by Erdman in some severe cases was considered to be a result of emboli in superficial veins. Localized superficial edema was ascribed to gas emboli in the lymphatic system. Erdman also referred to symptoms predominately affecting the respiratory and the gastrointestinal systems, noting that otherwise the abdominal visceral organs gave rise to no acute symptoms and that the sexual apparatus was unaffected except where there was spinal cord injury. Pain as well as more chronic disturbances of the bones, joints, and periosteum were described. Complications and late results of spinal cord injury such as cystitis and pyelonephritis were referred to. In the East River tunnels, there were 10 cases of permanent paralysis (0.3 percent of the total number of cases). Four of these died within 5 months from complications; 3 were lost sight of; and 3 were still suffering from spastic paraplegia when last examined.

4. RELATIVE FREQUENCY OF SYMPTOMS

It is universally agreed that muscular and joint pains are the commonest symptoms in

decompression sickness. For example, during the building of the Kehl bridge across the Rhine, François (*1169*) 1860 reported 32 cases of such pains in 20 to 25 men working in caissons which were sunk to 20 m. beneath water levels.

In a report published in 1900, Wainwright (*1173*), medical officer to the Baker Street and Waterloo Railway tunnel works in London, found that of 47 cases of caisson disease incident to this construction, there were 35 cases of pain in the knee joints, 11 of pain in the elbow, 7 of pain in the shoulder, 5 in the hip, 3 in the wrist, and 1 in the ankle. In 10 percent of the cases there were epigastric pain and vomiting. One case of itching of the skin and one of paraplegia involving the bladder and rectum were reported. All cases described occurred within 5 hours after emergence from compressed air and most of the cases developed within 2 hours. Resumés were given of 9 illustrative histories of workers suffering from compressed air illness after working at a gauge pressure of 30 lb.

In an analysis of 310 cases of caisson disease, Starr (*1172*) in 1909 found pain in the muscles of the back or in the extremities in 105 individuals. Ear affections, including rupture of the drum or symptoms comparable to Ménière's disease, were seen in 68 cases. Joint pains were complained of in 6 cases. Acute paraplegia occurred in 26 cases, 1 of which was that of a young engineer working on the Pennsylvania Railroad tunnel construction. Although accustomed to caisson operations, he was on one occasion decompressed too rapidly. Immediately on leaving the lock, he was seized with vertigo, intense headache, and pain in the joints. During the first 24 hours, there was delirium, restlessness, retention of urine, and difficulty in breathing. When seen on the fourth day, power of flexion and extention of the elbow was lost and there was numbness of the trunk and lower limbs. There was priapism, retention of urine and feces, and total anesthesia below the eighth rib. Respiration was diaphragmatic. The case presented the clinical picture associated with a transverse lesion, probably multiple in character, with its upper limits as high as the level of the fifth and sixth cervical segments of the cord. Although an unfavorable prognosis was expected, the patient went on to rapid recovery. After 2 months in bed, he was able to sit up and stand with help. Tendency to decubitus ulcers subsided within 6 weeks of the onset of the disease. Response to pin-prick and temperature sense returned before touch. Bladder control was not regained until the end of the second month. Four months after the onset, he was able to return to work.

Some cases of central nervous system involvement, according to Starr, show symptoms of spastic paraplegia while others present a picture of locomotor ataxia. More rarely, there is atrophic paralysis with disturbances of temperature and pain sense, the lesion being presumably in the gray matter of the cord. Some cases present symptoms in which all these conditions appear to be combined. In all these various types of spinal lesions as a result to exposure to rapid decompressions, recoveries have been recorded. Monoplegia observed by Starr in 17 cases, appeared to be cerebral rather than spinal in type. Symptoms of intense vertigo ascribed to emboli in the cerebellum were seen in 14 cases. These resembled in many respects Ménière's syndrome but were followed by paralysis of one or another of the cranial nerves suggesting that the origin of the symptoms was not in the inner ear. Thirteen of the 310 cases were characterized by asphyxia or by temporary aphasia, deafness, or temporary blindness.

In a report on 3,692 cases of caisson disease in the building of the East River tunnels,

Symptom	Number of cases	Percent
"Bends" (joint pain)	3,278	88.78
"Bends" with local manifestations	9	0.26
Pain with prostration	47	1.26
Central nervous system symptoms:		
1. Hemiplegia	4	0.11
2. Spinal cord symptoms	80	2.16
Vertigo ("staggers")	197	5.33
Dyspnea ("chokes")	60	1.62
Partial or complete unconsciousness	17	0.46

Keays (*1089*) in 1912 listed the following summary of relative incidence of various symptoms: (see Table on p. 119.)

Six of the cases of pain with prostration were fatal; 5 of the patients showing central nervous symptoms succumbed; and 9 in the category of partial or complete unconsciousness terminated fatally.

Erdman (*1067*) 1916 listed the chief symptoms of decompression sickness in the following order of frequency:

Symptoms	Percent of all cases
Pain in extremities or abdomen	88.00
Vertigo	5.00
Cerebrospinal symptoms	2.16
Dyspnea ("Chokes")	1.50+
Prostration of moderate degree with pains	1.25
Collapse with unconsciousness	.46

Levy (*2181*) in 1922 reported the following data comparing the relative frequency of various symptoms in cases encountered in the Public Service Commission tunnels and the earlier construction work on the Pennsylvania Railroad tunnels:

Symptoms	Percent of all cases on the Pennsylvania R. R. tunnels	Percent of all cases on the Public Service Commission
Localized pain	90.3	91.7
Vertigo	5.33	6.5
Central nervous system symptoms	2.16	1.6
"Chokes"	1.62	0.1
Partial or complete unconsciousness or collapse	0.46	0.1

In the Public Service Commission tunnel construction, there were 680 cases of compressed air illness out of a total of 1,361,461 decompressions. Of the 624 cases of localized pain, 49.3 percent (of the entire number of cases) complained of pain in only 1 joint. In 36.9 percent more than 1 joint was involved while in 5.6 percent there were body or head pains.

These data may also be found in Wright and Brady's article (*1162*) published in 1929. These authors also give a general summary of the principal symptoms and signs of the disease as well as a review of its incidence and mortality in various construction operations from the Douchy mines in 1839 to the Public Service Commission tunnel constructions in 1931.

The reader should also consult Lamanna's paper (*1170*) published in 1940 which describes caisson operations at Trieste, Italy. A description of 41 cases of compressed air illness is given in some detail. Forty-seven cases are grouped according to the following relative frequency of symptoms:

Symptoms	Number of cases	Percent of all cases
Pains in muscles and joints	22	46.8
Ear disturbances	14	29.8
Neurological symptoms	11	23.4

1168. Bertillon, [ ]. Construction du grand pont du Rhin; travaux exécutés dans l'air comprimé; effet de ce milieu sur les ouvriers: physiologie, pathologie et thérapeutique; prescriptions de l'hygiéne. *Un. méd., Paris*, 1861, Sér. 2, *10:* 346–350. [P]

1169. François, [ ]. Des effets de l'air comprimé sur les ouvriers travaillant dans les caissons servant de base aux piles du Pont du grand Rhin. *Ann. Hyg. publ., Paris*, 1860, Sér. 2, *14:* 289–319. [R]

1170. Lamanna, G. Contributo allo studio della malattia dei cassoni. *Rass. Med. Lav. industr.*, 1940, *11:* 443–482. [B, R, Ch]

1171. Shilling, C. W. The medical aspects of deep sea diving. *Conn. med. J.*, 1940, *4:* 597–599. [P, M, R]

1172. Starr, A. Caisson disease. *Med. Rec., N. Y.*, 1909, *75:* 1047–1049. [R, Ch]

1173. Wainwright, F. R. Observations on compressed air illness. *Lancet*, 1900, *2:* 1792–1799. [R]

5. TIME OF ONSET OF SYMPTOMS

While a few cases have been reported in which symptoms occurred during decompression, in most instances, the victims are attacked within a few minutes to some hours after leaving the caisson. In the East River Tunnel construction operation, 95 percent of the cases developed within 3 hours after leaving the compressed air lock. One percent were delayed over 6 hours and, of these, 4 somewhat

dubious cases were said to have occurred between 15 and 23 hours after decompression.

In explaining the variation in time of onset, Erdman (*1175*) 1913 refers to a statement by Paul Bert that gas bubbles do not form suddenly but continue to develop for some time after decompression. The onset is often quite sudden. A man may have worked for 3 to 4 hours in the tunnel or caisson; he emerges from the lock and starts for home. Fifteen minutes later, he may be attacked without warning with intense boring pains in the leg or abdomen or staggers and falls helpless to the ground, paralyzed from the waist down. If fortunate, he may be recompressed in a hospital lock within a few minutes of the attack. The pains vanish; the paralysis disappears; and the man may even return to his work the next day.

In a review on compressed air illness, Bassoe (*1174*) in 1910 noted that of 1,419 cases among 3,500 workers on the Hudson River tunnels (Erdman's cases) 43 percent developed symptoms within one-half hour after leaving the caisson while in 32 percent, the symptoms occurred within one-half hour to 1 hour after emerging. Thus, in 75 percent of all cases, symptoms supervened within 1 hour. Bassoe's article may also be consulted for a review of the incidence and mortality of caisson disease as reported by various investigators.

Of 680 cases occurring in the construction of the Public Service Commission tunnels in New York, 436 were accurately reported. Of these 436 cases, Levy (*2181*) 1922 reported that 280 or 64.2 percent developed within the first hour after decompression; 77 or 17.7 percent occurred in the second hour; 30 or 6.9 percent supervened in the third hour; 14 or 3.2 percent were stricken in the fourth hour; while 33 or 7.6 percent were attacked within the fourth to eighteenth hour. In the Pennsylvania tunnel operation records, it was noted that 85.9 percent of all cases developed symptoms in the first hour. Levy believed that this figure probably represented a closer approximation to the average than the figure of 64.2 percent for the Public Service Commission tunnels. He saw no cases in which the onset was delayed beyond 18 hours but noted that in the Pennsylvania tunnel records there were cases occurring 23 hours after decompression.

Stammberg (*2205*) in 1938 reported that cases characterized by the "bends" occurred within one-fourth to 8 hours after decompression. Cerebral disturbances including dizziness, headache, vomiting, and paralysis occurred within one-half to 2 hours after emergence from the caisson. Recompression brought relief but patients suffering from vertigo required in addition 1 or more days of bed rest. One case of special interest was reported by Stammberg, in which the patient showed symptoms of amnesia developing 8 days after the disturbing cause.

1174. Bassoe, P. Compressed air illness ("caisson disease"). *Illinois med. J.*, 1910, *17:* 462–469. [P, R]

1175. Erdman, S. The acute effects of caisson disease or aeropathy. *Amer. J. med. Sci.*, 1913, *145:* 520–526. [P, R]

6. GENERAL CASE HISTORIES

The following reports may be consulted by readers wishing to review representative case histories or additional data on the general symptomatology of caisson disease. Snell's report (*1191*) on the medical aspects of the Blackwall tunnel, published in 1897, discussed ear symptoms, pain in the extremities, paralysis, and Ménière's syndrome. The highest pressure in this construction was 52 lb.

Coleman (*1178*) in 1904 gave an account of symptoms occurring in tunnel workers in tunneling operations carried out in Lake Erie. The highest pressure attained was 46 lb. Decompression was carried out rapidly (in 1 to 3 minutes) and symptoms occurred within 10 minutes to 6 hours. There were excruciating pains, usually in the knees, sometimes in the joints, and rarely in the hips. Sometimes maniacal attacks occurred. Paraplegia lasting for a few hours to several months were reported and some patients were left with persistent spastic paraplegia. Bladder and rectal symptoms were reported as well as transient facial paralysis. Other cases were characterized by sensory disturbances, pruritus, bleeding from the nose and ears, vertigo, dimness of vision, headache, vomiting, muscular cramps, or acute attacks of dypsnea.

For a review of 11 cases of caisson disease occurring during the construction of foundations for the high level bridge over the Tyne in England, the reader is referred to a report by Parkin (*1129*) which appeared in 1905. This paper also contains a description of the physiological effects of compressed air and the general symptomatology of caisson disease. The author also discusses the possible analogy between compressed air illness and so-called "mountain" or "balloon" sickness.

For further case histories and descriptions of symptomatology, reports by the following authors should be consulted: Hermel (*1183*) 1863; Heiberg (*1182*) 1876; Friedrich and Tauszk (*1181*) 1896; Oliver, Smith, and Snell (*1189*) 1904; Brand (*1177*) 1905; Erdman (*1180*) 1912; Lapukhin (*1186*) 1913; Lerebeullet (*1187*) 1914; Hoskyn (*1184*) 1915; Aguglia (*1176*) 1920; Earl (*1179*) 1924; Sjöblom (*1190*) 1924; and Sudo and Horie (*1192*) 1928–29.

1176. Aguglia, E. Sù d'un caso di malattia dei palombari. *Riv. ital. Neuropat.*, 1920, *13:* 52–57. [Ch]

1177. Brand, J. D. Over ongevallen bij pneumatische fundeeringen. *Ned. Tijdschr. Geneesk.*, 1905, *41*(2): 34–40. [Ch]

1178. Coleman, J. B. Communication on caisson disease. *Brit. med. J.*, 1904, *2:* 1574. [Ch]

1179. Earl, R. Caisson disease resulting from complete disregard for the mandatory instructions of the diving manual relating to management of the diver's ascent in conformity with the decompression tables published therein. *Nav. med. Bull., Wash.*, 1924, *21:* 719–721. [Ch]

1180. Erdman, S. The acute effects of caisson disease. *Trans. fifteenth internat. Congr. Hyg.* (*Demogr.*), *Wash.*, 1912, *3*(2): 619–625. [P, R]

1181. Friedrich, V. and F. Tauszk. A caissonmunkások megbetegedéseiröl. *Orv. Hetil.*, 1896, *40:* 149–150; 162–163; 173–175; 186–188. [Ch]

1182. Heiberg, E. T. Sygdomsformer hos Arbejderne ved Fastbroanlaegget over Limfjorden. *Ugeskr. Laeg.*, 1876, Raekke 3, *22:* 377–386. [P, Ch]

1183. Hermel, E. *Des accidents produits par l'usage des caissons ou chambres à air comprimé dans les travaux sous-terains et sous-marins.* Paris, J.-B. Baillière et Fils, 1863, 96 pp. [C, Ch]

1184. Hoskyn, D. T. A case of caisson disease. *J. R. nav. med. Serv.*, 1915, *1:* 473–475. [Ch]

1185. Kühner, A. Caissonarbeiten. *Gesundheit, Lpz.*, 1895, *20:* 322–323; 339–340; 354–355. [Ch]

1186. Lapukhin, V. D. [Two cases of caisson disease.] *Nevrol. Vyestn.*, 1913, *20:* 655–664. [Ch]

1187. Lerebeullet, [ ]. Gli inconvenienti dell'aria compressa. *Gazz. Osp. Clin.*, 1914, *35:* 141–146. [P, R]

1188. Mummery, N. H. Diving and caisson disease. A summary of recent investigations. *Brit. med. J.*, 1908, *1:* 1565–1567. [P, R]

1189. Oliver, T., L. Smith, and E. H. Snell. Discussion on compressed-air illness, or caisson disease. *Brit. med. J.*, 1904, *2:* 317–321. [P, R]

1190. Sjöblom, J. C. Tvenne fall av dykaresjukdom. *Finska LäkSällsk. Handl.*, 1924, *66:* 398–404. [Ch]

1191. Snell, E. H. The Blackwall Tunnel from a medical point of view. *Hospital*, 1897, *22:* 126–127. [P, R]

1192. Sudo, S. and K. Horie. [A case of treated caisson disease.] *Bull. nav. med. Ass. Japan*, 1928–29, *17*(4): (Japanese text pagination), 19–22. (In Japanese.) [Ch]

7. PAINFUL INVOLVEMENT OF THE STRUCTURAL SYSTEM ("BENDS")

The first cases of "bends" in caisson workers were reported by Triger (*78*) in 1845. Two workers, after having passed 7 successive hours in compressed air suffered pains in the joints one-half hour after leaving the shaft. The first complained of severe pains in the left arm, and the second, of pains in the knees and left shoulder. In both cases, the painful symptoms were dissipated by rubbing the affected parts with alcohol. Triger's caisson penetrated to a depth of 25 m. under the river bed of the Loire.

Although "bends" were observed in these pioneer caisson operations, the first really scientific observations on caisson disease were made in 1854 by Pol and Watelle (*75*) who were the first to observe the disease in all its intensity in the mines at Duchy. Lewis (*1203*) 1860–77 reported pain and other symptoms in workers on the St Louis Bridge Company Project at Atchison, Kan. These workers were treated with ergot in conformity with the theory that the etiology is on the basis of vascular congestion. Lehwess (*1202*) in 1877 also described cases of joint pain and other symptoms in caisson workers at the Liteiny Bridge in Russia.

In 1882, Broughton (*1195*) reported the case of a foreman in the New York Caisson of a Hudson River tunnel who experienced pain

in the right knee on leaving the tunnel. The pain which radiated up to the hip and down to the ankle, was so severely acute that the patient was unable to remain quiet. After discussing his own personal experiences under pressures of 25 to 26 lb. per sq. in., Broughton reviewed some of Smith's work and considered the question of treatment.

In 1886, Pepper (*1207*) described a 35-year-old caisson worker who worked 8-hour shifts in a caisson under a pressure of 42 lb. Three weeks before, when seen by the author, he had suffered a severe chill on emerging from the caisson. In the week following, there was sweating, generalized pain, and headache with diarrhea and fever on the tenth day. Three days before the second examination, the patient had suffered a slight hemorrhage from the nose. Examination disclosed temperature elevation to 104° F., a pulse rate of 100, and a respiratory rate of 26. This patient does not appear to have shown typical symptoms of caisson disease. It seems quite likely that we are here concerned with "bends" complicated by an influenzal type of infection and the case is included here to indicate a possible error in diagnosis.

The reader is advised to consult the paper by Smith (*1210*) published in 1894 concerning medical problems which arose in the construction of a tunnel under the East River in New York at the foot of 72nd Street for the passage of gas mains. Workers carried out their labor at a pressure of 42 lb. and at the time of Smith's report, 21 cases had been admitted to Presbyterian Hospital; of these, 2 had died and 1 was suffering from paraplegia with little hope of recovery. A 29-year-old tunnel worker, who had labored in compressed air for 8 years without previous trouble, felt faint on emergence from the tunnel, and complained of difficulty in speaking and pain in the abdomen. Being a heavy drinker, he took several drinks of whiskey to assuage the pain. In about 10 minutes, the legs became numb and weak and within 20 minutes, the lower limbs were completely paralyzed. On examination, both legs were paralyzed, response to pin-prick and touch were lost in the limbs, the knee jerks were absent, and there was retention of urine with overflow. The next day, there was rectal paralysis with tympanites. The patient made a gradual improvement and 5 months after the accident, practically no anesthesia remained. He was still unable to control the bladder but normal bowel function had been re-established to some extent.

Smith noted that the pain usually appeared first in the lower extremities involving, within the next hour, the hips and often the lumbar and sacral regions. Since the pain was aggravated by the erect position, the victims often assumed a stooping posture. Such sufferers among the workers on the Brooklyn Bridge caissons in New York were the objects of good-natured and amused ridicule by their fellow workers. Their assumed postures gave rise to the term "bends" or "Grecian Bend," an allusion to the fashionable stoop in walking, common among women at the time the Brooklyn Bridge was being built.

Smith noted that pains in the epigastrium were common and that they might be associated with nausea and vomiting. Pains in the extremities were referred to the joints or the shafts of long bones. They were sometimes accompanied by tenderness on pressure but in other instances pressure gave relief. The pain fluctuated in intensity with a gradual or sudden onset. In some cases, the pains were comparable to the intense gastric crises of tabes dorsalis. Reflexes were either exaggerated or abolished. During paralysis the knee jerks were commonly increased. Paralysis was observed in a considerable proportion of cases generally affecting the lower limbs but the arms were not exempt. In some cases, an arm and leg on the same side were involved. The motor defects were either transient or persistent, partial or complete. The bladder and anal sphincter were usually affected at the same time. Sensory loss to pin-prick and heat and cold was usually observed in cases of paraplegia; pain was often persistent.

Silberstern (*1209*) in 1901 described muscle and joint pains as well as other symptoms. Shattuck (*1208*) in 1902 reported the case of a healthy young worker who suffered pains in the ankles and knees so severe that he could

not stand. The attack came on 15 minutes after a 10-minute decompression from his first day's work in compressed air. The patient was taken to hospital in a state of great suffering and prostration. He was treated with hypodermic injections of morphine and subsequently did well. The action of compressed air on the joints was described by DuBois-Reymond (*1197*) in 1906. In 1907, Klieneberger (*1200*) reported observations on 44 cases. In one, there was pain in the muscles and loss of motor power in the arms and legs for 8 days with vertigo and ataxic gait. In another case, there was severe pain in the extremities for 3 weeks. In a third case, there was severe pain in the extremities of 3 weeks' duration. In one instance, a worker "locked out" from a depth of 17 m. in 3 minutes and shortly after experienced pain in the lower half of the body, loss of motor power, ataxia, and difficulty of defecation and micturition. Some motor weakness in the lower limbs and ataxia persisted as well as exaggerated tendon reflexes and disturbance of deep sensibility. Another workman was decompressed from a depth of 17 m. in 10 minutes. Within a short time, he complained of pain and weakness of the legs and on the fifth day, there was fever, delirium, and coma. On examination, cutaneous hemorrhages were observed as well as paralysis of the extremities, ankle, and patellar clonus, and a positive Babinski sign. The bladder was paralyzed and examination of the fundi revealed optic neuritis and pathological foci in the retinae. This patient made a remarkable and complete recovery with the exception of slight fatigability of the lower extremities and increased tendon reflexes.

Grant (*1198*) 1898 reported cases of pain observed as medical officer to the Rotherhithe Tunnel Works. This construction operation was provided with a medical lock in which sufferers from caisson disease could be recompressed to the working pressure within 2 minutes. Decompression following therapeutic recompression was carried out over a period of about three-fourths of an hour. In ordinary decompressions, it was difficult to persuade the workmen to decompress slowly. The lock was small and 32 men were enclosed within a space of 470 cu. ft. The author himself was decompressed by one foreman at a rate of 15 lb. pressure in 1¾ minutes, in spite of definite instructions of a maximum rate of 5 lb. per minute. Admittedly, the conditions in the lock were unpleasant and the men were loath to remain there.

One workman 36 years old worked for 8½ hours in the tunnel at a working pressure of 16 lb. Ten minutes after emergence, he was seized by acute pains in the abdomen, the knees, and the ankles. Relief was obtained on reentering the tunnel. He reemerged from the tunnel in about an hour but on his way home, the pains returned again. He reentered the tunnel a second time. The abdominal pains were relieved but those in the knees and ankles persisted. He was given ergot and recompressed in the medical lock to a pressure of 16 lb. With this treatment, the pains gave way to numbness in the legs. The right foot dragged as he walked. On the next day, the paralysis of the legs was more definite on the right side with exaggeration of the knee jerks and some sensory loss. In 10 days, the patient was able to get around with the use of sticks. Three months later, he sought admission to the hospital because of the dragging of the right leg and 6 months later, he still required a stick to aid in walking. There was some wasting of the right thigh muscles and the right leg still dragged to some extent.

The onset of pain, according to Grant, does not always present a classical picture. For example, a workman of 45 years of age felt a slight pain in the left hip upon arising. He proceeded to work and found that the pain became worse upon locking in. The discomfort increased to the point where he left the lock and went home. Since there was no improvement, he returned to the works and entered the medical lock in which he was recompressed to 16 lb. and the air allowed to leak out slowly. Therapeutic recompression and decompression were repeated several times and finally the pains disappeared. However, they recurred again on his way home. When he was seen by Grant, the knee jerks were slightly exaggerated and the left leg dragged but no other signs were present.

Pains in the left hip and ankle incapacitated the patient for 2 weeks and at the end of this time, he returned to work. Another workman, aged 36, was seized with sharp pains in the back and legs on his way home from the tunnel. He spent a sleepless night, in this case doubtless due to the pain. Sleeplessness has, however, been observed as a symptom in compressed air workers even in the absence of pain. On examination, the knee jerks were exaggerated and ankle clonus could be elicited. The patient was treated in the hospital for over 2 months and then returned to work. Two weeks later, he suffered a similar attack with identical symptoms which kept him away from work for 1 month more.

Grant reported another case in which severe pains in the legs, back, shoulder, and elbows supervened shortly after leaving the tunnel. The patient dragged the right leg for approximately 10 days.

Lecaplain (*1201*) in 1914 described a patient of 31 years of age who was seized with violent pains in the head during the night after a day's work in the caisson. He had a sense of formication in all the limbs and the next day this developed into severe "bends" in the lower limbs with vomiting. When seen by Lecaplain, the patient had persistent pains in the knees, walking was difficult, and there was some deafness on the right side. On examination, the reflexes were exaggerated but no other signs were elicited. Three other cases were reported.

Johnston and Bradlaw (*1199*) in 1925 reported the case of a diver who made a rapid ascent due to fouling of the air line. He was submerged again and decompressed slowly but upon emergence showed symptoms of distressed breathing, cyanosis, sweating, dilated pupils, and pains in the arms, legs, and lower right abdominal quadrant. Twenty minutes later, he was placed in the recompression chamber and recompressed to the maximum pressure to which he was subjected during the dive. Relief was experienced when the pressure rose to half this level. The next day pains recurred in the shoulder, arm, and legs which lasted for 2 days. Nine days after the accident, he was discharged symptom-free.

O'Donnell's account (*1206*), published in 1929, of caisson disease in connection with the construction of the Liffey tunnel from 1926 to 1928 may be consulted for a description of the clinical aspects of caisson disease with particular reference to the "bends." In this construction, compressed air was used from April, 1927 to March, 1928. The tube which was built for the transmission of cables and mains was 830 ft. long and only 7 ft. in diameter. The shafts on each side were just over 100 ft. deep. Of 69 workers employed in the construction, 29 suffered from caisson disease, a very high incidence. The working pressure ranged from 25 to 30 lb. and shifts were 3 to 4 hours' long. A workman of 45 (new to "high air") with a systolic blood pressure of 110 and a pulse rate of 72 on prior examination, worked for one shift. On his way home he was seized with severe pains in the legs and arms and spent most of the following 36 hours in the medical lock, emerging occasionally to test his progress. He worked in the tunnel the following morning but had a recurrence of pain in one arm. He was again fit for work 2 days later but was advised to change his occupation.

A man of 58 who had been a compressed air worker at intervals for 30 years, with a blood pressure of 150/110, suffered severe "bends" in the knees. A week later he suffered another extremely severe attack lasting almost 24 hours. He resumed work 6 days later but, at the end of a month, suffered an acute attack of abdominal pain with vomiting on return home from work. He was well within a few days but wisely decided to confine himself to surface work. Another workman, aged 40, also new to compressed air work and with a blood pressure of 140/110, worked for 1 day on the north shaft of the tunnel. He then worked on the south side where the air was damp and cold. After the first shift on the south side, he complained of excruciating pains in the hip and abdomen. After prolonged and fruitless recompressions, he was taken to the hospital. Two days later he was free of pain but when seen 3 months later still complained of some pain in the shoulder and knees.

It is clear from these cases that "bends" pain may exist without other symptoms and

that it may be transitory or leave the patient with permanent, painful symptoms in joints or muscles.

A new workman of 32, with a blood pressure of 120/80, complained of joint pains 1 week after starting work. He was unrelieved by recompression treatment. On being admitted to the hospital, he was found to have urinary retention and paralysis of the lower part of the body. He left the hospital after 1 month with a well-defined spastic paraplegia; the knee jerks were exaggerated, there was a positive Babinski sign on both sides, and ankle clonus could be elicited. This case is remarkable in that the pressure in the tunnel at that time was only 23 to 24 lb. per sq. in. O'Donnell believed that damp conditions in the tunnel definitely increased the risk and severity of caisson disease at pressures usually associated with a negligible incidence of the disease. He considered that individuals with a systolic blood pressure of more than 130 mm. Hg, unless experienced compressed air workers, were not satisfactory for this type of work. Compressed air work, he believed, is essentially an occupation for young men of good physique and temperate habit.

Abadir (*1193*) in 1933, as medical officer on the Kasr El Nil Bridge in Egypt, observed no symptoms in the workers at gauge pressures up to 15 lb. except ear pains on compression, normally to be expected. Above 20 lb., he observed, in addition to other symptoms, pains in the muscles of the forearms and legs as well as in the wrists, elbows, hip, and knee joints. In more severe cases, there was swelling of the muscles. Such pain usually disappeared spontaneously within a few hours but sometimes it lasted for 3 to 4 days.

Joint pains were also reported by Molfino (*1205*) in 1937, and Manabe (*1204*) in 1938 described a case with severe pain in the muscles. Donald (*1196*) in 1944 reported the case of a diver who worked at a depth of 40 ft. for 2 hours and surfaced in 1 minute. Five minutes later he complained of pain in the region of the upper left premolar tooth. Since the pain was very severe, he was returned to a depth of 18 ft. and decompressed over a period of 30 minutes. The pain increased in severity and anesthesia of the gums and teeth in the upper left maxillary region developed. He was recompressed to 12 lb. and decompressed at a rate of 8 minutes per lb. Symptoms again returned. Recompression the third time was to 13 lb. with a decompression rate of 12 minutes per lb., after which he was relieved and had no further symptoms.

As is the case in compressed air workers, decompression sickness at high altitudes is characterized by symptoms of pain. Bridge, Henry, Cook, Williams, Lyons, and Lawrence (*1194*) 1944 have analyzed 167 man-runs made by 80 subjects, doing 10 step-ups every 5 minutes for 90 minutes in decompression chambers at a simulated altitude of 38,000 ft. Eighty man-runs (50.9 percent of all man-runs) ended prematurely in forced descent. A major cause was pain in the joints (68.2 percent of the descents). "Chokes" accounted for 8.2 percent of the descents while a further 8.2 percent descended because of abdominal gas pains. Nine and five-tenths percent of the descents were caused by muscle pains, syncopal reactions, etc. Joint pains, with or without descent, occurred in 62.3 percent of all man-runs and were reported equally on both sides of the body. Pain in the knee, the joint most frequently affected, occurred in 53.9 percent of all man-runs. There was a high incidence of pain in the anterior portion of the knee and if any knee pain recurred, it was likely to appear in the same knee. Moderate or severe "chokes" were associated with joint pains in a significant number of instances. Post-flight symptoms referable to the joints affected at altitude occurred subsequently in more than 15 percent of all man-runs. Nearly 26 percent of all those complaining of joint pain at the simulated altitude had trouble with these joints during the post-flight hours. Nearly one-half of these symptoms were in the nature of joint swelling which the authors thought probably due to synovial or bursal effusions. Post-flight symptoms were reported for a few joints and muscles not affected at altitude.

1193. Abadir, F. Caisson disease on the new Kasr El Nil bridge. *J. Egypt. med. Ass.*, 1933, *16*(2): 811–825. [Ch]

1194. Bridge, E. V., F. M. Henry, S. F. Cook, O. L. Williams, W. R. Lyons, and J. H. Lawrence. Decompression sickness. Nature and incidence of symptoms during and after artificial decompression to 38,000 feet for ninety minutes with exercise during exposure. *J. Aviat. Med.*, 1944, *15:* 316–327. [M]

1195. Broughton, M. The "bends." *Med. Trib.*, 1882, *4:* 185–195. [R, Ch]

1196. Donald, K. W. A case of compressed-air illness. *Brit. med. J.*, 1944, *1:* 590. [Ch]

1197. DuBois-Reymond, R. Über die Wirkung des Luftdrucks auf die Gelenke. *Arch. Anat. Physiol., Lpz.*, (Physiol. Abt.), 1906, pp. 397–400. [P]

1198. Grant, C. G. A few cases of compressed-air illness, with remarks. *Brit. med. J.*, 1908, *1:* 1567–1568. [Ch]

1199. Johnston, J. E. and A. S. Bradlaw. A case of caisson disease. *J. R. nav. med. Serv.*, 1925, *11:* 293–295. [Ch]

1200. Klieneberger, [ ]. Luftdruckerkrankungen beim Bau der grünen Brücke. *Dtsch. med. Wschr.*, 1907, *33:* 1316–1318. [Ch]

1201. Lecaplain, [ ]. Accidents de l'air comprimé au cours des travaux de reconstruction du viaduc d'Eauplet. *Normandie méd.*, 1914, *29:* 288–301. [Ch]

1202. Lehwess, [ ]. Statistische Mittheilungen über die Erkrankungen der Arbeiter beim Liteiny-Brückenbau, speciell derjenigen, welche in den Caissons unter hohem Luftdruck arbeiten. *St Petersb. med. Wschr. (Z.)*, 1877, *2:* 298–299. [R]

1203. Lewis, G. L. The effects of compressed air upon the human system. *Trans. Kans. Acad. Sci.*, 1860–1877, *1:* 279–291. [R]

1204. Manabe, K. A case of severe caisson disease. *Bull. nav. med. Ass. Japan*, 1938, *27*(10): (Japanese text pagination), 661–666; (English text pagination), 60–61. (In Japanese with English summary.) [R]

1205. Molfino, F. Sulle forme artralgiche della malattia dei cassoni. *Rass. Med. Lav. industr.*, 1937, *8:* 92–98. [R]

1206. O'Donnell, F. J. Caisson disease. As experienced in the construction of the Liffey Tunnel (1926–28). *Irish J. med. Sci.*, 1929, Ser. 6, No. 45: 618–622. [Ch]

1207. Pepper, W. Caisson disease; the treatment of sub-acute and chronic rheumatism. *Med. Bull., Philad.*, 1886, *8:* 239–242. [Ch]

1208. Shattuck, F. C. Caisson disease. *Boston med. surg. J.*, 1902, *146:* 414. [Ch]

1209. Silberstern, P. Hygiene der Arbeit in komprimierter Luft. *Handb. Hyg.* (Suppl.), 1901, *1:* 75–108. [P, B, R]

1210. Smith, A. H. Caisson disease. *Med. Rec., N. Y.*, 1894, *45:* 130–133. [P, R, Ch]

1211. Anon. Influence de l'air comprimé sur la santé. *Ann. Hyg. publ., Paris*, 1845, Sér. 1, *33:* 463. [C, Ch]

8. PULMONARY INVOLVEMENT

Attacks of dyspnea and oppression in the chest (known among compressed air workers as the "chokes") usually accompany a grave clinical picture. In many of the case histories referred to in this section, symptoms of dyspnea and tightness in the chest are described. Two case histories will be cited here. The first is an atypical case reported by Thost (*1213*) in 1909. In this case, there was tightness in the chest and sweating while the patient was still at work. Bleeding from the mouth and nose occurred on locking out and the patient suddenly lost consciousness. On regaining his senses, he was deaf in the right ear and complained of headache and dizziness. Oliver (*1212*) in 1899 described a patient of 45 years of age who was working in a caisson on the bed of the Tyne at a depth of 77 ft. below the water level. On emerging from the caisson, he felt giddy; there was numbness in the legs and he vomited and fell unconscious. The next morning, he got up to go to work but had severe epistaxis and again collapsed. While unconscious he perspired freely; the pulse was slow and full. There was dyspnea without cyanosis. On regaining consciousness, he complained of severe muscle pain, throbbing in the head, and a sense of oppression and tightness in the chest. The knee jerks were exaggerated and for several days there was pain in the muscles and weakness of the legs, but no urinary or rectal disturbance. At times there was a wandering delirium. At the time the case was reported, progress to recovery was satisfactory, although there was still some weakness of the limbs.

1212. Oliver, [ ]. Man suffering from caisson disease or compressed air illness. *Northumb. Durh. med. J.*, 1899, *7:* 8–11. [R, Ch]

1213. Thost, A. Über Caissonkrankheit. *Fortschr. Med.*, 1909, *27:* 69–71. [Ch]

9. INVOLVEMENT OF THE INTEGUMENT

Ginestous and Cruchet in 1921 (*1214*) reported a case of subconjunctival hemorrhage developing in a diver after a shallow dive, and Mellinghoff in 1934 (*1216*) reported lividity of the skin. This occurs in association with many of the serious cases of decompression

sickness and has been interpreted as being due to air embolism of the cutaneous vessels. Areas of superficial swelling and subcutaneous emphysema with crepitation have also been seen in occasional cases. Most of the earlier workers describing caisson disease have observed mottling, bruising, marbling, or lividity of the skin, both in cases which terminated fatally and in victims who subsequently recovered. Superficial ulcers of the leg as a complication of caisson disease were reported by Glasser (*1215*) in 1943.

1214. Ginestous, [ ] and [ ] Cruchet. Ecchymose sous-conjonctivale chez un scaphandrier (accident de travail). *Gaz. hebd. Sci. med.*, 1921, *42:* 44. [Ch]

1215. Glasser, S. T. Leg ulcers as a complication of caisson disease. *Surg. St Louis*, 1943, *14:* 302–305.

1216. Mellinghoff, K. Hauterscheinungen bei Caissonkrankheit. *Z. klin. Med.*, 1934–35, *127:* 457–459.

10. DISTURBANCES OF THE CENTRAL NERVOUS SYSTEM AND THE AUTONOMIC NERVOUS SYSTEM

(a) Motor and Sensory Disturbances

There is a large body of literature on the motor and sensory disturbances which form a prominent feature of the clinical picture of caisson disease. As previously stated, the symptomatology is usually complicated. Babington and Cuthbert (*1218*) in 1863 described cases of paralysis in men following compressed air work in sinking the foundations of Londonderry New Bridge. One patient became ill upon reaching the open air after working for 4 hours at a pressure of 23 lb. He lost consciousness immediately and the surface of his body was cold and livid. The right side of the face was paralyzed with strabismus of the right eye. The pulse was weak and irregular and the rate about 150. The respiratory rate varied between 24 and 42. The patient died in 24 hours. Another workman was seized with severe pains in the legs and thighs some hours after leaving the caisson and was unable to walk. The legs were cold, and without sensation, as revealed by the patient burning his toes without pain. He recovered within 2 days. Another patient collapsed in the air lock. When seen, he was in a semicomatose condition which lasted for 18 hours. On regaining consciousness, he was found to be paralyzed below the level of the fourth rib. There was retention of urine and complete loss of sensation and movement. Death occurred after 160 days from widespread bed sores. In another case similar to this, death came after 30 days. A similar case was reported by Limonsin (*1258*) in 1863.

Bauer (*1222*) in 1870 also called attention to pathological effects upon the spinal cord of men decompressed from increased atmospheric pressures in connection with the construction of the bridge across the Mississippi River at St. Louis. In many cases there was pain and general hyperesthesia in the lower half of the body, followed by numbness. In some instances, the symptoms disappeared at this stage or developed into paralysis of the lower extremities. In some cases, there were choreiform movements and muscular rigor. In the hospitalized cases the paraplegia varied from a light paresis to complete paralysis. Retention of urine was reported.

Eads (*1243*) in 1871 also described cases of paralysis occurring among workmen on the St. Louis bridge project. Of historic interest is the "treatment" of caisson disease referred to by Eads, that of wearing bands of alternate scales of zinc and silver in the form of chain mail around the wrists, arms, ankles, and waist, and also sometimes on the soles of the feet. These metallic bands were believed to act as a battery, delivering small currents and so preventing painful symptoms.

Schultze (*1274*) in 1880 reported a case of paraplegia with a post-mortem study of spinal pathology. This patient had been working at pressures of about 4 atmospheres (absolute) for some time. On emerging from the caisson after a shift of 6 hours, he suffered pain in both ankle joints, and within 20 minutes, developed a complete paralysis of the lower extremities. On admission to a hospital, both limbs were completely paralyzed and he was unable to sit up. There was paralysis of the bladder and rectum and disturbance of sensation up to the level of the umbilicus. He developed decubitus ulcers, cystitis, and pyelitis and died 2½ months after the accident. During his illness, the motor paralysis remained unchanged but sensation improved. At autopsy, there were

revealed whitish, irregular, spotty, degenerated areas in the white columns of the spinal cord. These lesions were mainly limited to the lower dorsal region and localized in the posterior and lateral columns. Microscopically, the degenerated areas showed complete disappearance of nerve fibers with thickening of the blood vessels. The gray matter in the cervical and lumbar areas was intact, while in the dorsal region of the cord, there was some degeneration in a circumscribed area on one side only. Schultze observed no tearing of the cord substance. It should be noted, however, that in Schultze's case, death was delayed.

Charpentier (*1240*) in 1883 reported the case of a diver examined 9 years after an accident to his diving suit. The suit had ruptured at the neck after he had been on the bottom for 12 minutes. He felt strangled and lost consciousness in which state he was brought to the surface. The face was swollen and cyanotic and he remained unconscious for 3 weeks. On recovering consciousness, there was complete paralysis of the limbs without pain. When seen 9 years later by Charpentier, he presented the clinical picture of locomotor ataxia with fulgurant pains in the lower extremities, motor incoordination of the legs, back pain, girdle sensation, gastric crises, and sensation of thoracic constriction.

Further reports on the neurological manifestations of caisson disease were published by Rosendo Pi (*1270*) 1887; Catsaras (*1234*, *1235*, *1236*, *1237*) 1888, 1889, and 1890; von Hallerstein (*1249*) 1889; and Nixon (*1262*) 1889. The latter reported the case of a diver in whom sensation and movement of the lower extremities were lost immediately after ascent. Sensation returned in a short while but the patient suffered repeatedly from vertigo, numbness and tingling in the legs. On examination about 3 months after the dive (which was to a depth of 143 ft.), the patient was able to walk only with difficulty and the gait was waddling. On standing, chronic twitches were observed in the quadriceps muscles and the patellar reflexes were exaggerated. The plantar reflexes were normal but the cremasteric reflex was abolished. There was some sensory impairment and also residual impairment of bladder function.

Van Rensselaer (*1350*) in 1891 described 2 cases coming to his attention. In the first there was complete paraplegia of both lower extremities and loss of bladder and rectal control. There was partial improvement commencing first with the toes and extending upward. Control of the bladder was regained after 4 months, but after 1 year there was still moderate spastic paralysis. The second patient died about a month following an accident in a caisson under the Hudson River. The patient, who had never previously been in compressed air, remained in the caisson about half an hour. The times of locking in and locking out were not recorded. Upon emerging, he complained of dizziness, weakness, nausea, and tinnitus. In a few minutes he fell unconscious. Upon recovery of consciousness, there was complete paralysis in the lower half of the body with urinary retention and persistent constipation. The patient developed, in the course of the following month, widespread gangrenous areas in the sacral region, thigh and calf, and urinary tract infection. In the lower dorsal region, at autopsy, there was found an area of degeneration in the posterior and lateral columns of the white matter of the spinal cord. Above and below this lesion, ascending and descending degeneration were observed.

For further cases of diver's paralysis and other neurological manifestations of caisson disease, the reader may consult reports by Watson (*1281*) 1893; Grasset and Rauzier (*1248*) 1894; Maidlow (*1261*) 1895–96; Bignami (*1224*) 1897; Hoche (*1251*, *1252*) 1897 and 1898; Fürstner (*1245*) 1898; Gaudoin (*1246*) 1898; Taylor (*1276*, *1277*) 1898; and Cayley and Douglas-Powell (*1238*) 1898.

The case reported by Taylor (*1277*) presents features of special interest. The patient was a diver who had suffered three previous attacks of paralysis of the lower limbs. The accident in question occurred on the fourth descent of the day. The diver had made three previous descents to 162 ft., remaining on the bottom for 20 minutes and rising to the surface in 6 minutes. On the fourth descent, he was jammed against an iron beam and was unable to rise. After 5 minutes' time, he felt suffocated and began to lose consciousness. He

was finally freed and was rapidly drawn to the surface. Upon surfacing, he became giddy and sick and complained of numbness in the feet and arms. On examination, at Guy's Hospital, London, 9 weeks later, there was loss of power in both legs; no wasting of the muscles was evident but they were soft and flaccid. Partial anesthesia was noted over the inner sides of both legs. There was no loss of sensation to pin-prick and the response to hot and cold stimuli was normal.

A patient reported by Lépine (*1256*) 1899 had worked in caissons for about 6 months without difficulty. On September 30, 1898, a caisson in which he was working at a pressure of 3 to 3.5 atmospheres (absolute) exploded. He escaped to the surface but very shortly complained of pain in the loins; presently paralysis of the legs as well as loss of sensation in the lower limbs was evident. There was also urinary incontinence. Fifteen days later, he was capable of some movement of the lower part of the body and sensation began to return. Bladder difficulties persisted and there was also constipation. At the end of the second month, the patient could walk a little but the initial flaccid paralysis had given way to contracture. There were also girdle pains. The bladder and rectal difficulties ceased but the patient did not make much further progress. At the time of the report, his gait was hesitant and uncertain; the feet dragged on walking and there were tremors in the legs. Some atrophy was present. Sensation of touch, heat, and cold, was diminished in both legs. Tendon reflexes were exaggerated and there was knee and ankle clonus. The cremasteric reflex was abolished and the plantar reflex was weakly flexor. The lesion was considered to be hemorrhagic and located in the lumbosacral region.

von Schrötter (*1273*) in 1899 reported bradycardia as a common manifestation in caisson disease, often associated with neurological signs and symptoms. Sometimes, however, it may exist alone and in some cases may persist for a long period. A report by von Schrötter (*1272*) in the same year refers to 200 cases of caisson disease. He believed that the neurological manifestations were not due to hemorrhage in the cord or to tears within the central nervous system but rather to ischemia associated with liberation of gas bubbles in the fine vessels of the central nervous system.

Cases of caisson disease were also reported by Maguire (*1260*) 1899–1900, Lépine (*1257*) 1900, and Ladd (*1254*) 1902. The latter report is of special interest in that the patient was submerged for several hours in cold water in a tunnel with not only severe "bends" but also profound shock from the exposure to cold. The rectal temperature at one stage was as low as 30° C., but in spite of this, the patient made a complete recovery. Several reports of typical case histories were given by Hill and Macleod (*1250*) in 1903. In these cases, neurological manifestations were permanent. This paper should also be consulted for a particularly graphic account of the symptoms of caisson disease as given by one of the workmen in the Blackwall tunnel in London.

Previous reports of Boinet and Audibert (*1229*, *1230*) in 1904, and a longer review by the same authors (*1231*) in 1905 should be examined for a consideration of caisson disease, particularly as it affects sponge and coral divers. Case histories are given as is a detailed table recommending duration of descent, times of work at the bottom, ascent rate, minimal rest intervals, and number of dives per day. Boinet and Audibert noted that sudden death may occur almost immediately after return to normal pressures or during the acute phase of the disease within a few hours after onset. The most common motor disturbances are paraplegias involving the lower extremities; these may be permanent or transitory, recovery may be complete or partial, and the patient may be left with complete functional loss or severe disturbances of function, or the residual deficit may be minimal. Rarely there may be hemiplegia with facial paralysis or aphasia.

Another case of caisson disease in a sponge diver was reported by Bondet and Piéry (*1232*) in 1905. This patient, 25 years of age, came to the hospital with a 9-month history of paralysis of the lower limbs. Nine months previously, he had made three dives to a depth of 72 m. in a single day. On removing his helmet at the termination of the last dive, he felt a sense of warmth in the abdomen and

became nauseated and vomited. He complained of pounding in the ears and he was unable to walk. He then fell unconscious. Four hours later on regaining his senses, all four limbs were paralyzed. There were spasms and pains in the lower limbs and he complained of thirst. Function was restored in the arms in 15 days but he was left with persistent flaccid paralysis of the lower limbs, retention of urine, and diarrhea. The bladder and rectal disturbances lasted for 1 month. By the fifth and sixth month, he began to walk. On examination 9 months after the accident, there was extreme contracture of the lower limbs and the patient walked with difficulty. The knee jerks were exaggerated and there was a positive Babinski sign on both sides, but no appreciable muscular atrophy. Sensory loss was complete in the lower limbs and trunk except that he had a feeling that his legs were cold. He was not aware of the position of his limbs in bed and vibratory sense was absent in the lower part of the body; micturition and defecation were involuntary. No abnormal signs were elicited from the upper limbs. Bondet and Piéry considered that the lesion was probably an area of hemorrhage and necrosis located no higher than the second dorsal segment of the cord and involving the pyramidal tracts and all of the sensory columns. The patient had had a similar accident 4 years previously from which he had made an apparently complete recovery in 6 days.

Recovery was reported in a case of caisson disease by Oliver (*1264*) in 1905 and a case with chronic neurological signs, including foot drop, was published by Patrick (*1268*) in 1905. Other cases with neurological sequelae were reported by Audibert (*1217*) 1906, Barrington (*1220*) 1906, Boinet (*1227*, *1228*) 1906, Ellis (*1244*) 1906, Kropveld (*1253*) 1908, Wondra (*1282*) 1908, Blick (*1225*) 1909, Pagano (*1266*, *1267*) 1909 and 1910, Ryan (*1271*) 1909, Wassermeyer (*1280*) 1909, Paditzky (*1265*) 1910, Spaar (*1275*) 1910, Pérez-Vento (*1269*) 1912, Veselitsky (*1279*) 1912, Bérillon and Gosset (*1223*) 1913–14, Cannady (*1233*) 1916, Lantieri (*1255*) 1921, de Crecchio (*1242*) 1932, Noica and Pârvulescu (*1263*) 1933, Boenjamin (*1226*) 1937, and Gotten (*1247*) 1939. Gotten reviewed the neurological manifestations of caisson disease and referred to a case of amaurosis with choked discs.

Cases with girdle pains and symptoms and signs of locomotor ataxia have been referred to. For further reports, the reader should consult case histories by McCune (*1259*) 1908 and Charpentier (*1241*) 1883.

As has been stated, the neurological disturbances in caisson disease may range from transient paresthesia to complete sensory or motor loss or both with grave sequelae. It is remarkable, however, how complete a functional recovery may be achieved even in cases of gross disorder of function. Transitory disturbances of spinal function were discussed by Catsaras (*1235*) in 1889 and this paper merits detailed study. Three remarkable cases of functional recovery were reported by Thompson (*1278*) in 1894. The first of these was a caisson laborer, aged 38, who had worked for many years in compressed air. He had often suffered from extreme pains in the lower extremities but never from paralysis. Six days before admission to hospital and shortly after leaving the caisson, he suddenly lost all power of movement and all sensation in both legs. Motor power partially returned within a day or two but since he found himself unable to empty his bladder, he sought relief at the hospital. There he was catheterized and could empty the bladder voluntarily at the end of a week. Three weeks after the accident, he walked easily and was discharged recovered. The second case was a patient of 33 who had worked for 14 years as a compressed air worker. Five to six years previously he had suffered several attacks of anesthesia and parasthesia in the extremities upon leaving the caisson which had lasted for several hours. The night before admission to the hospital and about 15 minutes after leaving the caisson in East River, N. Y. where he had been working at a pressure of 4 atmospheres (absolute), he experienced pain in the right leg. It should be noted that the decompression time was extremely rapid, being not more than 5 minutes. Within an hour he experienced such severe lancinating pains in both legs that he was unable to walk. He developed partial paralysis

of both legs and greatly exaggerated knee jerks, but at the end of the fourth day was completely recovered. The third case was that of a compressed air worker of 25 years of age who suddenly lost the use of both legs and left arm on leaving the caisson. Hearing was completely lost in the left ear and he complained of dull pains in the head and abdomen with vomiting. Deafness and paralysis disappeared after 3 days and at the end of 3 weeks, he was completely recovered and returned to work.

A case of paraplegia with recovery on the following day was described by Barrington (*1219*) 1905, and Baske (*1221*) 1929 described the case of a diver who was paralyzed in both legs and had, in addition, disturbances of bladder function but who recovered in approximately 6 days.

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(b) Convulsive Seizures

In rare cases, patients exhibit various types of convulsive movements of the body. For example, Scott (*1287*) in 1878 reported a case of a diver who, on ascending from a depth of 144 ft., exhibited clonic spasms of the limbs. In addition, there was a feeling of constriction

about the waist and pain in the spinal region. Loss of bladder and rectal control also supervened. In a case reported in 1896 by Silberstern (*1288*) the patient developed dyspnea, cramps, and fell unconscious. There were tonic and clonic convulsive movements of the extremities and episthotonus as well as spasm of the glottis. The patient was recompressed to a pressure of 2.3 atmospheres (absolute) and artificial respiration was administered. Under this treatment, the spasms disappeared and consciousness returned.

Holzinger (*1286*) in 1900 reported a case of a caisson worker who had worked at a depth of 20 m. He was "locked out" in 8 minutes. Shortly after leaving the caisson, there were sudden loss of consciousness and generalized convulsions recurring until the next day. The left lower extremity was paralyzed. After 2 weeks, the patient left the hospital with a minimal spastic paresis of the left leg and foot and patellar clonus. The patient gave no previous history of epilepsy. Holzinger's report also contains other cases and may be consulted by readers wishing to add to their familiarity with the clinical literature.

One of the most remarkable clinical histories of a patient with caisson disease was that reported by Zervos (*1290*) in 1903. The report concerns a patient 38 years of age who had been a sponge diver for a considerable time. He had always been in good health and there was no history of epilepsy. The patient lost consciousness on removing his diving suit and experienced 2 or 3 generalized convulsive seizures at intervals of 10 to 15 minutes. He finally regained consciousness and was taken to his home. That evening, he was seen by Zervos and seemed perfectly well. However, just as the doctor was about to leave, he was called back as the patient had been seized with another generalized convulsion involving tonic spasms of the face, arms, and legs. The pupils were widely dilated, respiration was suspended, and the face was typically cyanotic. The convulsion lasted about one-half minute, leaving the patient in a comatose condition breathing stertorously. Fifteen to twenty minutes later, he had still another attack and there were repeated seizures during the next 2 hours. They gradually diminished in intensity and became more and more widely spaced although they continued throughout the night. The next morning, the unfortunate patient lay comatose, the face cyanotic and livid. Breathing was slow, irregular, and shallow and the pulse small, thready, and rapid. The temperature had fallen to 36.8°C. Zervos administered an injection of ether and caffeine, never doubting that his patient was about to breathe his last. However, about 11:00 a.m. there was a definite improvement. The skin was of better color, respiration was more ample and deeper, and the pulse was stronger and slower. However, he was still unconscious. Further injections of ether and caffeine were given and toward evening the patient's clinical condition was further improved. He was able to protrude his tongue if asked to do so very loudly but unable to make replies. The next day improvement was maintained and continued and he was able to speak a few words. On the following day, he opened his eyes and could speak. There was no trace of motor or sensory defect and within several days, he had made a complete recovery. Obviously, the pathological process in this remarkable case was localized within the upper levels of the central nervous system and in contrast with the usual situation, did not involve the spinal cord. It is extremely difficult to explain adequately just how so rapid a recovery was possible.

Boinet and Audibert (*1284*) in 1904 called attention to a case in which complete paraplegia supervened about 10 minutes after emergence from the caisson. There were also sensory disturbances of the legs and the trunk to the level of the umbilicus. After about a month, the patient walked with a spastic gait and there was incontinence of urine and feces. Patellar reflexes were exaggerated and the patient became a victim of epileptiform convulsions. Boinet, Piéri, and Isemein (*1285*) in 1925 referred to the case of a sponge diver who lost consciousness shortly after ascent. When examined, he was delirious, the lower limbs were paralyzed as was also one side of the face. The patient exhibited convulsive attacks and periods of dementia and died

after a few hours. Convulsions were also seen in a case reported by Anderson (*1283*) in 1927. This patient had spent 7 minutes at a depth of 33 ft. in a diving helmet. On emerging from the water, he complained that the right arm and leg were paralyzed and that breathing was difficult. Within a short time, he was seized with tonic and clonic convulsive movements involving the right arm and leg and the neck and back. These convulsions were irregular but followed each other in close succession. The next day, there was some return of motor power and that evening he was placed in a recompression chamber. The pressure was raised to 22 lb. and then lowered again to zero in about 35 minutes. Two days later, symptoms were still not alleviated. He was recompressed again, this time to a pressure of 75 lb. for about 5 minutes and then decompressed by stages lasting over a period of about 3 hours and 37 minutes. Three days later, he was discharged without symptoms.

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1284. Boinet, [ ]. and [ ]. Audibert. Les paralysies des scaphandriers. *Marseille méd.*, 1904, *41:* 693–694. [Ch]

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(c) Cerebral Symptoms

In addition to convulsive manifestations, many of which may be cerebral in origin, a few cases have been reported in which patients suffer from psychic and other disturbances referable to lesions in the cerebral cortex. In 1889, Catsaras (*1292*) referred to various mental disturbances in divers, and Chazal (*1293*) in 1905 described hysteria and neurasthenia provoked by working in compressed air. Psychotic symptoms in a caisson worker were described in 1933 by Kluge (*1296*). Oka (*1297*) in 1935 reported 2 cases in which the main symptom in each was aphasia. Both patients were caisson workers on the Nerbudda bridge under construction by the Hindustan Construction Company in India. The first patient had been working 5 or 6 hours daily for 6 days. Two days after his last shift in the caisson, he had fever and there was incoherent speech. By the sixth day, he could make no sound. Tongue movements were normal and examination of the central nervous system was negative. The pulse rate was 74 without irregularity. On recompression in the medical lock, his apathy vanished, hearing was improved, and on return to the lock 2 days later, full power of speech was restored and maintained. The second case was that of a coolie, aged 28 years, who had worked 5 or 6 hours daily for the previous 3 months in the air lock. Three days before admission, he had had a cough and a rise of temperature. Upon admission he was strikingly apathetic, muttering at random. The sputum was blood-stained, the pulse was feeble, and the temperature below normal. Mental incoherence lasted for about 8 days. He developed spastic paraplegia from which he recovered although speech was completely lost. While the second case is doubtless a clear-cut example of caisson disease with the excessively rare symptoms of parmanent aphasia, there is real doubt as to whether the speech loss in the first case may not be attributable to psychological causes not related to pressure effects. In both of these cases, the diagnosis is difficult and some infection of the central nervous system may have well been the underlying cause of the symptoms in the second case.

An unusual case of compressed air illness was referred to by Francis (*1295*) in 1943. In this case, symptoms developed 30 minutes after stage decompression from a pressure of 122 lb. in a test run in a compression chamber. The patient was dizzy and the pupils dilated. He could see newspaper print clearly but the

words had no meaning. There were presumably no other positive clinical findings. He was recompressed to 89 lb. per sq. in. and kept at this level for 30 minutes. He was then taken by stages back to zero pressure; the total decompression occupying 143 minutes. From a level between 28 lb. and zero, he breathed oxygen. The patient was normal on emergence and there was no recurrence of symptoms. This case, exhibiting symptoms of word-blindness, appears to be unique in the literature on the clinical aspects of compressed air illness.

Cerebral symptoms occur not only after decompression from pressures greater than 1 atmosphere but also in decompression to high altitudes. Engel, Webb, Ferris, Romano, Ryder, and Blankenhorn (*1294*) in 1944 described a migraine-like syndrome complicating decompression sickness in subjects exposed to simulated altitudes. Patients exhibited scintillating scotomata and there were focal neurological signs and headaches. Electroencephalographic observations on two subjects showed electrical abnormalities originating in discreet cortical areas corresponding to the clinical localization of the neurological disturbances. These electroencephalographic abnormalities disappeared with the fading of the scotomata. It was considered that these symptoms probably originated from spasm of cerebral arteries and that they were probably not due to gas emboli.

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1293. Chazal, Paul. *Contribution à l'étude de l'hystéro-neurasthénie traumatique. Le syndrome hystéro-neurasthérique provoqué par le travail à l'air comprimé.* Thèse (Méd.) Paris, Henri Jouve, 1905, 99 pp. [P, R]

1294. Engel, G. L., J. P. Webb, E. B. Ferris, Jr., J. Romano, H. Ryder, and M. A. Blankenhorn. A migraine-like syndrome complicating decompression sickness. Scintillating scotomas, focal neurologic signs and headache; clinical and electroencephalographic observations. *War Med., Chicago,* 1944, *5:* 304–314. [R]

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1297. Oka, M. G. Two cases of caisson sickness presenting 'aphasia' as one of the chief symptoms. *Indian med. Gaz.*, 1935, *70:* 629–630. [Ch]

11. SUDDEN DEATH AND DEATH IN THE ACUTE PHASE

As has been stated, victims of decompression sickness may be apparently close to death and yet survive. On the other hand, victims do occasionally drop dead suddenly or succumb within an hour or two after exhibiting acute symptoms. A case of death in the acute phase from compressed air illness was reported in 1930 by Ghose (*1299*), resident medical officer on the River Hooghly tunnel under construction by Messrs. John Corcoran and Sons, Ltd. (Westminster, London) near Calcutta. This worker, a man of 20, was seized with generalized pain mostly in the knee joints and abdomen. There was also paralysis in the legs and vomiting. When seen, he was in a semiconscious condition; there was mottling of the skin over the chest and subcutaneous emphysema in the abdominal region. The knee jerks could not be elicited nor could the pulse be felt at the wrist. He was recompressed twice and appeared to improve. However, improvement was not maintained and he died during the second recompression. At autopsy by the local police surgeon, the subcutaneous tissue of the chest and abdominal wall was found to be crepitant and filled with air. The cavities of the heart, particularly the right ventricle, were congested with blood and filled with gas bubbles. The lungs, liver, spleen, kidney, and brain were congested. In the spinal cord, microscopic areas of hemorrhage were reported at various levels. This patient was new to compressed air and had worked during that day for 2 shifts of 3 hours each at a pressure of 3.5 atmospheres (absolute). The fatality occurred after emerging from a third shift in the caisson. Fatal cases have also been reported by Archambeault (*1298*) in 1923, Shimoyama (*1301*) 1930, and Haaland and Schaanning (*1300*) in 1932. It should be borne in mind that sudden death rarely occurs in caisson and tunnel workers. These cases are to be distinguished

from sudden fatalities occurring after rapid ascents as, for example, in submarine "lung" escapes. The clinical picture and etiology of these latter cases are discussed under the section on "lung" accidents in individual submarine escape (p. 223).

1298. Archambeault, C. P. A fatal case of caisson disease. *Nav. med. Bull., Wash.*, 1923, *19:* 167–168. [Ch]

1299. Ghose, N. N. Death from compressed-air sickness in India. *Indian med. Gaz.*, 1930, *65:* 698–699. [Ch]

1300. Haaland, M. and C. K. Schaanning. Ddsfall hos dykkere. *Med. Rev., Bergen.*, 1932, *49:* 260–276. [R]

1301. Shimoyama, M. (Cases of caisson disease with a fatal case caused by a derangement of diving-bell.) *Bull. nav. med. Ass. Japan*, 1930, *19*(5): (Japanese text pagination), 44–48. (In Japanese.) [Ch]

12. SPECIAL EFFECTS ON THE CARDIOVASCULAR SYSTEM

It is quite apparent that the heart and circulation are involved in all cases of caisson disease. As may be seen by consulting the section on the physiology of decompression (p. 38), gas bubbles have been found within the heart and blood vessels both experimentally and clinically. According to Swindle (*1346*) 1937 and End (*2548*) 1938, intravascular agglutination of erythrocytes occurs as a result of rapid decompression. This may possibly be the primary disturbance in caisson disease.

1302. Viguier, [ ] and G. Jean. Embolie gazeuse de l'artère fessière (accident de décompression). *Bull. Acad. Méd. Paris*, 1918, *80:* 377–378. [Ch]

C. INCIDENCE, DIAGNOSIS, AND PROGNOSIS OF DECOMPRESSION SICKNESS

A number of considerations bearing upon the differential diagnosis, incidence, prognosis, and mortality of decompression sickness have already been discussed in the foregoing sections. For further reference to these problems, the reader is invited to consult reports by the following authors: Smith (*76*) 1873; Bert (*16*) 1878; Van Rensselaer (*1350*) 1891; Heller, Mager, and von Schrötter (*20*) 1900; Snell (*1148*) 1896; Oliver (*1122*) 1905–6; Hill (*1083*) 1912; Keays (*1089*) 1912; Erdman (*1067*) 1916; Levy (*2181*) 1922; Wright and Brady (*1162*) 1929; Singstad (*39*) 1936; and the comprehensive review of Shilling (*1141*) 1938.

D. ETIOLOGY OF DECOMPRESSION SICKNESS

Very soon after the introduction of the caisson, it began to be apparent that the characteristic symptoms of so-called caisson disease were associated with too rapid decompression. Development of the disease was determined by the pressure to which workmen were subjected and the duration of exposure. Many theories have been advanced to explain the etiology of caisson disease and our knowledge of the pathological process is greatly advanced. However, the etiology is not yet irrefutably established. For critical reviews of the various theories that have been proposed to explain the cause of caisson disease, reference should be made to Van Rensselaer's paper (*1350*) 1891 and to two articles by Shilling (*1141*, *1142*) 1938 and 1941. Other discussions of the etiology of caisson disease are to be found in reports by the following authors: Granjon-Rozet (*1324*) 1880, Gruber (*1326*) 1895, Kropveld (*1331*) 1908, Martini (*1334*) 1933, Desoille (*1317*) 1937, and Reghizzi (*1339*) 1939. In regard to the gas embolism theory and the recent hypothesis advanced by End (*2548*) 1938 that intravascular agglutination of the erythrocytes appears to be the primary disturbance in caisson disease, reference may be made to the section on the physiological effects of decompression from pressure higher than 1 atmosphere (p.38).

A number of bizarre hypotheses have been advanced to explain the etiology of caisson disease. Bouchard (see *1141*) 1869 believed that the condition was due to the compression and expansion of abdominal gases. On compression, the intestinal contents were diminished in volume so that the abdominal wall was supposed to act like a "cupping glass" and blood was drawn into the abdominal vessels. On decompression, blood was forced by expansion of abdominal gases into various other organs of the body where vessels were deprived of their tone. It was considered that the vessels might rupture and produce hemorrhages. MacMorran (see *1141*) 1902 considered that in caisson disease, there was hyperemia of nervous cen-

ters arising from mechanical pressure and that carbon dioxide elimination was interfered with. This hypothesis was criticized in 1902 by Hepburn (*1327*). Theories of etiology of caisson disease were reviewed in 1902 by Abbamondi (*1303*) who held that rapid decompression was a cause of "tissue damage." Macnaughton (*1333*) 1906 believed that caisson disease resembled a nonfatal lightning stroke and that the air of the caisson was full of what the author termed "hydro-electricity" arising from friction of air along the walls during changes in pressures. This electricity was supposed to be carried throughout the caisson by droplets of water vapor and resulted in excess nervous stimulation which manifested itself in motor or sensory reactions such as the "bends." Conroy (*1316*) 1910 revised an earlier hypothesis in suggesting that caisson disease is due to a toxemia resulting from excessive catabolism. The question of whether exposure to high pressure raises metabolic rate has been largely answered in the negative and, moreover, the theory of excessive metabolic breakdown resulting from raised atmospheric pressure does not explain how workers can withstand many hours in the caisson only to fall victim of the disease shortly after decompression; nor does Conroy's theory account for the effectiveness of recompression therapy in treating the "bends."

Theories of the causation of caisson disease may be classified into three groups: (a) the theory of exhaustion and cold, (b) the theory of mechanical congestion with sequelae, and (c) the gas embolism theory. The exhaustion theory was proposed and advocated by Bouhy (see *1141*) 1848, Barella (*1046*) 1868, Woodward (see *1141*) 1881, and others. It was first believed that the pains from which caisson workers suffered were of a rheumatic nature caused by rapid chilling of the air during decompression at a time when the workmen were tired and their bodies bathed in sweat. The exhaustion theory was insufficient to explain the phenomena observed and, in addition, it was found that in other circumstances exposure to much lower temperatures and even greater degrees of fatigue were borne without symptoms of caisson disease. Although exhaustion may be a contributory factor in the development of caisson disease, it clearly does not sufficiently explain the etiology.

The mechanical congestion theory has had many advocates and Van Rensselaer (*1350*) 1891 supported this view. It was held that peripheral blood vessels were constricted or compressed during exposure to raised atmospheric pressures and blood was, therefore, driven to the interior of the body and especially to those organs protected by a bony casing from the external pressure. It has been repeatedly shown, however, that raised atmospheric pressures act uniformly on all parts of the body and there is no differential mechanical effect on the circulation. However, Guerard (see *1350*) 1854, Limousin (see *1350*) 1863, and others believed that the viscera and brain became congested by "black blood." This congestion was believed to be the immediate consequence of compressed air forcing the blood mechanically from the compressible peripheral tissues into the deep-lying, practically incompressible internal organs. This central influx of blood and consequent visceral congestion was believed to be harmless during exposure to raised atmospheric pressure, because the blood absorbs and holds in solution more than its usual amount of oxygen. Thus, although the circulation was abnormal, yet the tissues received a sufficient supply of oxygen. However, on decompression, the effete matter of the blood was supposed to produce pernicious effects. Tissues were believed by this mechanism to be deprived of oxygen.

Boucquoy (*1055*) 1861 advanced the view that the visceral congestion occurring as a result of compression was complicated on decompression by evolution and liberation of gas in the internal organs and tissues. This liberated gas might rupture small capillaries and cause hemorrhages and death might be due to gas emboli in the lungs. Babington and Cuthbert (*1218*) 1863, Febvré (*1320*) 1879, and others advanced a theory of congestion followed by hemorrhage on decompression. It was considered that distended internal vessels might be ruptured by pressure of blood being forced into them from the peri-

phery. This theory does not fit all the facts. Van Rensselaer pointed out that hemorrhage and extreme congestion have been found from other causes and that the condition was never sufficient to cause paralysis.

Several workers, notably Moxon (see *1350*) 1881 and Twynam (*1436*) 1888 believed that on decompression, there was a rush of blood from congested internal organs to the empty external vessels, leaving the internal organs a prey to dangerous anemia. It was believed that the lesions within the central nervous system in particular were due to this acute revulsive anemia. This ingenius theory fails, however, to account for the fact that the spinal cord is not anemic in cases of caisson disease that come to autopsy but is invariably congested. The theory was, however, advanced as late as 1890 by Ball (*1305*).

According to Van Rensselaer (*1350*) 1891, the theory of congestion followed by comparative stasis appeared to be the most valid explanation of caisson disease. Smith (*76*) 1873, Nixon (*1262*) 1889, Knapp (*1093*) 1891, Edelheit (*1318*) 1896, Snell (*1148*) 1896, Porter (*1134*) 1907, and others also supported the theory. It was believed that engorged internal vessels became paralyzed by overdistention during compression. This was thought to lead to a comparative stasis in the internal organs including the central nervous system. Van Rensselaer concluded that after prolonged exposure to raised atmospheric pressure, the vessels of the central nervous system and other organs became congested and were unable to empty themselves. The circulation was slowed and thrombi might be formed. The extent and permanency of symptoms was believed to depend upon the degree of stagnation. The longer the duration of high pressure, the more severe the damaging effects upon the dilated vessels of the viscera and the greater the vasomotor paralysis. According to Van Rensselaer, this comparative stasis of the blood in the internal organs leads to malnutrition of the tissue, particularly the spinal cord.

The gas embolism theory of the etiology of caisson disease is the most acceptable hypothesis at the present time. However, as Shilling (*1142*) 1941 has stated, there are a number of facts difficult to reconcile with the gas bubble theory. As has long been known, decompression, both from raised atmospheric pressures to normal and from normal barometric pressure to pressures less than 1 atmosphere, will result in the liberation of free gas in the blood and tissues of animals and human beings. The important question is whether or not this liberation of gas is the etiological factor. Boyle gave a clear account of aeroembolism in 1670 (*2565*) and van Musschenbroek (*56*) 1739 confirmed Boyle's observations. In 1857, Hoppe (*1329*) found that rats withstood decompression from 1 atmosphere to a pressure of 50 mm. Hg (absolute) at which pressure the animals suffered from convulsive seizures. The rats succumbed at pressures between 40 and 50 mm. Hg and at autopsy free gas was found in the great veins leading to the heart and the right auricle and ventricle. Hoppe attributed sudden death in compressed air workers to the liberation of gas from the blood and tissues during decompression. This hypothesis was greatly advanced by Paul Bert (*1306*) 1872, and it was also supported by François (*1169*) 1860, Leyden (*1380*) 1879, Shewen (*1342*) 1881–82, Cassaët (*1311*) 1886, Catsaras (*1312*, *1313*) 1889, and many others.

Catsaras' and Bert's experiments and case histories were reviewed by Altschul (*1304*) 1895, and Silberstern (*1343*, *1344*) 1895 and 1896 also discussed the etiology of caisson disease. The latter article contains an excellent bibliography. The view that the symptoms of caisson disease were due to the formation of gas bubbles during too rapid decompression was also accepted by Zuntz (*1352*) in 1897. von Schrötter (*1340*) 1899 also favored the gas embolism theory as did Oliver (*1336*) 1906.

Nitrogen saturation and desaturation in caisson disease were discussed by Gallivan (*1321*) in 1907, and Brooks (*1309*) 1907–8 also concluded from animal experiments that the cause of caisson disease is the rapid liberation of air from fluids and tissues of the body. The composition of gas emboli formed during decompression has been investigated by Heller, Mager, and von Schrötter (*28*) 1900.

The gas bubble theory was also accepted by Oliver (*1337*) 1908, Grimbach (*1325*) 1909, Silberstern (*1345*) 1909, McWhorter (*1335*) 1910, Lereboullet (*1332*) 1913, and Keyser (*1330*) 1916.

In 1922–23, von Schrötter (*1341*) again reviewed the question of the etiology of caisson disease with particular reference to bubble formation as a cause of lesions in the spinal cord. The gas embolism theory was also discussed in 1925 by Branco (*1308*).

The Hoppe-Bert theory was accepted by Clark (*1315*) 1893. However, he believed that peripheral vessels were almost completely emptied under the effects of high pressure, so that blood gases were more easily affected by changing pressures. Clark's views are discussed in two papers by Hodgen (1328) 1870–71 and Clark (*1314*) 1870–71.

Fahr (*1319*) 1940 found that mice, in distinction to guinea pigs, did not get caisson disease on being suddenly decompressed from 3 atmospheres (absolute) after a 1½ hours' stay at this pressure. Fahr concluded from this that in addition to the release of gas bubbles on sudden decompression, there are also mechanical lung changes such as alveolar tears and aspiration of air into the open venous capillaries and that these play a part in the causation of caisson disease. While mice showed no symptoms and no lesions on sudden decompression from 3 atmospheres or from 6½ atmospheres, guinea pigs died of typical caisson disease after sudden decompression. In the latter animals, there was paralysis of the lower extremities and then of the whole body followed by apnea and a few minutes later by cardiac arrest. Gas was found in the heart, pulmonary veins, and the superior and inferior venae cavae. There was also gas in the coronary and mesenteric vessels. Tears were seen in the alveoli of the lungs. Fahr called attention to a description of human fatalities from caisson disease reported by Hoppe in which there were hemorrhage and rupture of the smallest vessels. It was Fahr's belief that nitrogen is released from solution in the blood too slowly to cause sudden death and Fahr considered that the tears in the substance of the lung were caused by expansion of air in the lungs on decompression and the difficulty of exhaling excess air rapidly enough. (Further discussion of the effects of air under raised intrapulmonary pressures in causing air embolism in the blood will be found in the section on gas embolism (p. 221).

It was found by Fahr that guinea pigs, injected subcutaneously with atropine to dilate the bronchioles, supported a pressure of 6½ atmospheres for 1½ hours and showed a great delay of symptoms on subsequent decompression. The author, therefore, considered that in guinea pigs the symptoms of caisson disease are associated with bronchial spasm leading to trapping of air in the alveoli. Expansion of this air was believed to cause tears and result in the entry of air into the blood. In some cases, Fahr was able to prevent caisson disease in guinea pigs on accelerating the respiratory rate by administration of carbon dioxide in the compressed air. He noted that the respiratory rate in the guinea pigs is slower than that in the mouse and considered the possibility that rapid respiration in the mouse may save it from caisson disease.

The question of the etiology of caisson disease is linked with the problem of the causation of decompression sickness in aviators. Harvey and his colleagues have made valuable contributions to our knowledge of bubble formation both at high altitudes and under conditions of decompression from raised atmospheric pressures. For a discussion of this work, the reader is referred to a paper by Harvey (*378*) published in 1945. The relation of bubble formation to aviators' "bends" and the effect of denitrogenation by pre-flight oxygen inhalation in preventing decompression sickness have been discussed by Webb, Engel, Romano, Ryder, Stevens, Blankenhorn, and Ferris (*1351*) 1944; and a critical evaluation of recent investigations of aeroembolism was published by Carson (*1310*) in 1942. For a further discussion of decompression sickness as it relates to aviators, the reader may consult appropriate sections in the bibliographies published by Hoff and Fulton (*3*) 1942 and Hoff, Hoff, and Fulton (*4*) 1944.

Shilling (*1142*) 1941 found the often very long interval between decompression and development of symptoms a fact difficult to explain on the gas bubble theory alone. He also considered variation in susceptibility in the same individual under identical working conditions to be a fact tending to prevent ready acceptance of the gas embolism theory. Also, after prolonged exposure to high pressure beyond the maximum calculated saturation time, it was impossible to desaturate safely according to the standard tables. This indicated, according to Shilling, a discrepancy not covered by the gas embolism theory.

In 1938, End (*2548*) advanced the view that agglutination of erythrocytes appears to be the primary disturbance in compressed air illness and that bubble formation may be looked upon essentially as a serious complicating factor. End stated that rapid decompression in experimental animals caused exaggerated agglutination of the cells within the blood vessels and even when it was impossible to demonstrate any gas bubbles in the body, some of these animals showed vascular infarcts. Swindle (*1346*) 1937 demonstrated that increased carbon dioxide will cause an increase in the extent and duration of intravascular agglutination, whereas alkalization and oxygen administration tend to diminish or prevent agglutination just as they tend to diminish or prevent caisson disease. Unpublished observations of End and van Hecke indicate that there is a fall in the carbon dioxide combining power of the blood during prolonged compression. This, according to these authors, may explain why the difficulty on decompression increases even after complete saturation with nitrogen (because of the increased tendency toward acidity of the blood which favors agglutination). End does not, however, believe that the importance of bubble formation can be denied and states that if it is severe, it may dominate the clinical and post-mortem picture.

A number of factors have been advanced as predisposing causes in caisson disease. These include obesity, age, alcoholism, diseases of the heart, lungs and kidneys, fatigue, and excessive dampness and foul or vitiated air. Regarding the effect of contaminated air in contributing to the incidence of caisson disease, papers by Thomson (*1347*, *1348*) 1912 and 1913 may be consulted.

1303. Abbamondi, L. Studio sulle cause che possono determinare sinistri accidenti nei palombari. *Ann. Med. nav. colon.*, 1902, *1:* 693–719. [R]

1304. Altschul, A. Beitrag zur Kasuistik der Taucherkrankheiten. *Wien. med. Wschr.*, 1895, *45:* 2020–2026. [R]

1305. Ball, J. B. Caisson or tunnel disease. *Lond. med. Recorder*, 1890, *3:* 241–242. [R]

1306. Bert, P. Sur les effets de l'air comprimé, les accidents qu'il occasionne, leur cause et les moyens d'y remédier. *Bull. Soc. méd. Yonne*, 1872, *13*(2): xlviii–lv. [C, R]

1307. Boyle, R. Continuation of the observations concerning respiration. *Philos. Trans.*, 1670, *5:* 2035–2056. [C]

1308. Branco, C. Accidentes pelo ar comprimido. *Trib. med., Rio de J.*, 1925, *29:* 121–127.

1309. Brooks, H. An experimental study of caisson disease. *Proc. N. Y. path. Soc.*, 1907–08, N. Ser., *7:* 58–87. [R]

1310. Carson, L. D. A critical evaluation of recent investigations of the phenomenon of aero-embolism. *Nav. med. Bull. Wash.*, 1942, *40:* 284–290. [R]

1311. Cassaët, Jean-Eric-Theodote. *De la pathogénie des accidents de l'air comprimé.* Thèse (Méd.), Bordeaux, Imprimerie Vve Cadoret, 1886, 110 pp. [P, R]

1312. Catsaras, M. Recherches cliniques et expérimentales sur les accidents survenant par l'emploi des scaphandres. III. Pathogénie. *Arch. Neurol., Paris*, 1889, *18:* 80–109. [P, R]

1313. Catsaras, M. Recherches cliniques et expérimentales sur les accidents survenant par l'emploi des scaphandres. IV. Etiologie, *Arch. Neurol., Paris*, 1889, *18:* 207–243. [P, R]

1314. Clark, E. A. A reply to Professor Hodgen's so-called "review" of my report of the "bridge cases." *Med. Arch., St Louis*, 1870–71, *5:* 295–300. [R]

1315. Clark, H. E. On caisson disease, with some speculations as to its causation. *Glasg. med. J.*, 1893, *40:* 17–28. [R, Ch]

1316. Conroy, P. Etiology of caisson-disease. *Marit. med. News*, 1910, *22:* 330–334. [R]

1317. Desoille, H. Pathologie des scaphandriers. *Pr. méd.*, 1937, *45:* 1809–1810. [R]

1318. Edelheit, S. Physikalische Erklärung der Caissonkrankheit. *Ärztl. CentAnz.*, 1896, *8:* 257–259.

1319. Fahr, E. Experimentelle Untersuchungen über das Wesen der Caissonkrankheit. *Zbl. allg. Path. path. Anat.*, 1940, *75:* 257–261. [P, R]

1320. Febvré, Alphonse. *Expériences comparatives sur la décompression brusque et sur l'injection d'air dans les artères.* Thèse (Méd.) Nancy, Imprimerie Berger-Levrault et Cie, 1879, 41 pp. [R]

1321. Gallivan, J. V. The etiology of caisson disease. Theories based on clinical observations of the disease. *Long Is. med. J.*, 1907, *1:* 181–184. [R, Ch]

1322. Gersh, I., G. E. Hawkinson, and E. N. Rathbun. Tissue and vascular bubbles after decompression from high pressure atmospheres—correlation of specific gravity with morphological changes. *J. cell. comp. Physiol.*, 1944, *24:* 35–70.

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1324. Granjon-Rozet, [ ]. *Étude sur l'étiologie des accidents observés chez les hommes travaillant dans l'air comprimé.* Thèse (Méd.) Paris, A Parent, Imprimeur de la Faculte de Medecine, 1880, 61 pp. [R]

1325. Grimbach, R. Zur Kasuistik der pneumatischen Erkrankungen. *Zbl. inn. Med.*, 1909, *30:* 1169–1176. [R, Ch]

1326. Gruber, M. Zur Aetiologie der Caissonkrankheit. *Öst. Sanitätsw.*, 1895, *7:* Beil., 111–119. [R]

1327. Hepburn, M. L. Caisson disease. *Brit. med. J.*, 1902, *1:* 1179. [R]

1328. Hodgen, J. T. Effects of compressed air upon the human body. *Med. Arch., St Louis*, 1870–71; *5:* 219–226. [R]

1329. Hoppe, F. Ueber den Einfluss, welchen der Wechsel des Luftdruckes auf das Blut ausübt. *Arch. Anat. Physiol., Lpz.*, 1857, pp. 63–73. [Ch]

1330. Keyser, T. S. Compressed air disease, with notes on a case and discussion of etiology from the standpoint of physical laws. *Cleveland med. J.*, 1916, *15:* 250–255. [R, Ch]

1331. Kropveld, A. De nieuwste theorie ter verklaring van een groep verschijnselen voorkomende bij caissonziekte. *Ned. Tijdschr. Geneesk.*, 1908, *44:* 1211–1212. [R]

1332. Lereboullet, P. Les accidents de l'air comprimé. (Séméiologie et pathogénie.) Progr. méd., Paris, 1913, *29:* 587–593. [R]

1333. Macnaughton, G. W. F. Frictional electricity: a factor in caisson disease. *Lancet*, 1906, *2:* 435–436. [R]

1334. Martini, R. Della malattia dei cassoni. *Med. d. Lavoro*, 1933, *24:* 201–215. [R]

1335. McWhorter, J. E. The etiological factors of compressed-air illness. The gaseous contents of subaqueous tunnels; the occurrence of the disease in workers. *Amer. J. med. Sci.*, 1910, *139:* 373–383. [R]

1336. Oliver, [ ]. La maladie des caissons. *Bull. med., Paris*, 1906, *20:* 437–439. [R]

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1338. Quincke, H. Experimentelles über Luftdruckerkrankungen. *Arch. exp. Path. Pharmak.*, 1909–10, *62:* 464–493. [R]

1339. Reghizzi, A. C. Contributo clinico alle malattie professionali dei cassoni. *Arch. ital. Otol.*, 1939, *51:* 408–420. [R]

1340. Schrötter, [ ]. Patologia delle malattie da rapida decompressione. *Ann. Med. nav. colon.*, 1899, *5:* 97. [R]

1341. Schrötter, H. von. Zur Pathogenese der Schädigungen des Zentralnervensystems, insbesondere des Rückenmarks nach rascher Dekompression beim Menschen. *Psychiat.-neurol. Wschr.*, 1922–23, *24:* 253–255. [P, R]

1342. Shewen, A. Caisson fever, so called. *Aust. med. Gaz.*, 1881–82, *1:* 116–117. [R]

1343. Silberstern, P. Zur Casüistik der Caissonkrankheit. *Wien. med. Wschr.*, 1895, *45:* 1305–1308. [P, R]

1344. Silberstern, P. Zur Casuistik und zur Prophylaxe der Caissonkrankheit. *Wien. med. Wschr.*, 1896, *46:* 1894–1898; 1942–1945. [P, R]

1345. Silberstern, [ ]. Die Berufsarbeit der Caisonarbeiter. *Mschr. Unfallheilk.*, 1909, *16:* 266–267. [R]

1346. Swindle, P. F. Occulsion of blood vessels by agglutinated red cells, mainly as seen in tadpoles and very young kangaroos. *Amer. J. Physiol.*, 1937, *120:* 59–74. [P, R]

1347. Thomson, T. K. An unsuspected cause of caisson disease. *Int. Congr. Hyg. (Demogr.)*, 1912, *15*(3): 608–610. [P, R]

1348. Thomson, T. K. Caisson disease. *Med. Brief.*, 1913, *41:* 283–284. [R]

1349. Van Rensselaer, H. The pathology of the caisson disease. *Med. Rec., N. Y.*, 1891, *40:* 141–150; 178–182. [B, R]

1350. Van Rensselaer, H. The pathology of the caisson disease. *Trans. med. Soc. St. N. Y.*, 1891, pp. 408–444. [B, R]

1351. Web, J. P., G. L. Engel, J. Romano, H. W. Ryder, C. D. Stevens, M. A. Blankenhorn, and E. B. Ferris, Jr. The mechanism of pain in aviators' "bends." *J. clin. Invest.*, 1944, *23:* 934–935. [R]

1352. Zuntz, N. Zur Pathogenese und Therapie der durch rasche Luftdruckänderungen erzeugten Krankheiten. *Fortschr. Med.*, 1897, *15:* 632–639. [R]

1353. Anon. Caisson work *Industr. Med.*, 1934, *3:* 42–43. [R]

E. PATHOLOGICAL LESIONS

1. POST-MORTEM FINDINGS

Although Paul Bert contributed richly to our understanding of the physiology of de-

compression sickness, he made very few observations on the actual pathological changes resulting from exposure to air under high pressures. Subsequent investigations have added extensively to our knowledge of the morbid anatomy of caisson disease, diver's paralysis, and experimental decompression sickness in animals; and since these studies may contribute to a better understanding of the nature of the pathological process involved and thus lead to more effective prophylaxis and treatment, they will be reviewed and critically examined in this section.

The evidence available from post-mortem examinations of workers dying after exposure to high atmospheric pressures is limited, to some extent, by the incompleteness of the autopsies performed; also, in many instances the necropsy was conducted after some hours or days so that post-mortem autolysis and putrefactive gas formation may have obscured the pathological picture. In 1878, Heiberg (*1357*) reported the results of an autopsy carried out on a worker dying within a few hours of a fulminating attack of caisson disease, at the bridge construction on the Limfjord. The report states that there were no signs of putrefaction and that the skin of the chest, abdominal wall, and back were covered with multiple, livid, reddened patches. The skin was also emphysematous to the touch. On opening the inferior vena cava, an extensive clot was extracted which was filled with trapped air bubbles of varying sizes. Air bubbles were also found within the clotted blood of the right ventricle and the lungs were congested. Air could also be expressed from the cut surfaces of the liver and spleen, and the intestines and pyramids of the kidneys contained air. No bubbles were seen in the brain or in the spinal cord on close examination, but a thrombus was found in the lower lumbar region.

Altschul in 1895 (*1354*) cited several cases of paralysis, particularly of the lower limbs in divers coming rapidly to the surface. In an attempt to elucidate the pathological physiology of diver's paralysis, Altschul kept a dog at a depth of 43½ m. below sea level for 5 minutes, bringing it rapidly to the surface in 1 minute's time. In this animal, large numbers of air bubbles were present in the chambers of the heart; the blood vessels of the cerebral hemispheres and the cerebellum were charged with bubbles. Occasionally, air bubbles were also seen to be present in blood vessels of the spinal cord and in the cerebrospinal fluid. The blood in the liver, spleen, and kidneys likewise contained air; and foamy blood was expressed from the lungs. A hemorrhagic infarct was observed in the left lung.

An important contribution to the knowledge of the cause of death in compressed air workers was made in 1897 by Heller, Mager, and von Schrötter (*1358*) who discussed the symptoms of acute decompression sickness and case histories with post-mortem findings. A workman of 31 years of age had worked in the caisson under a pressure of 3.2 atmospheres (absolute) for 6 to 10 hours. On reaching the lock he apparently felt well, but one-half hour later complained of pains in the hands and feet which became rapidly more severe. There was dyspnea and rapidly developing cyanosis, terminating in death approximately 2 hours after "locking out." On post-mortem examination 32 hours after death, the meningeal vessels were seen to contain small air bubbles. Little abnormality was observed macroscopically in the brain and spinal cord. Hemorrhagic areas were observed in the vocal cords, the bronchial mucosa, and in the pericardium. The main pathological finding was an acute edema with extensive hyperemia of the lungs. In the author's second case, that of a worker 40 years of age, the victim had worked during the previous 11 months in caissons at pressures of 3.3 to 3.6 atmospheres (absolute) for a total of 2,072 hours. On April 1, 1896, after work at 3.3 atmospheres (absolute), he was stricken with severe pains on leaving the caisson. He was recompressed in the hospital lock to 3 atmospheres (absolute) for 1 hour and then uniformly decompressed over a period of 40 minutes. The patient was relieved for about three-fourths of an hour and then the pains returned with greater intensity than before. On the last day, the pains continued and during the night he expired and was found dead. An autopsy performed 21 hours

later revealed small hemorrhages in both lungs and air bubbles in the right ventricle of the heart. The abdominal viscera showed marked and extensive congestion. On naked eye examination, nothing abnormal was found in the spinal cord, but microscopic sections indicated the presence of gas bubbles in the capillaries and finer arteries and veins.

In 1898, Schäffer (*1363*) reported autopsy findings in caisson workers killed when the caisson was suddenly decompressed from 3.5 atmospheres (absolute) to normal pressure. Three workers who had been in the chamber for 4 hours were instantly killed. Autopsies were carried out 22 hours after death. In the first case, the blood from the skin incision was found to be filled with fine air bubbles. Bubbles were also found in the minute vessels of the large and small intestines and the vessels of the spermatic cord were also seen to contain gas bubbles. Free gas was present in the abdominal cavity and within the chest; bubbles were also observed in the internal mammary arteries and veins. Bubbles were also present over the pleura and within the coronary arteries. The lungs and heart were congested as were also the esophagus and larynx. Punctate hemorrhages were found in the tracheal mucosa down as far as the bifurcation of the trachea. The spleen was enlarged and congested, and from the cut section frothy blood could be squeezed in large quantities. Frothy blood was also present in the cortex and medulla of the kidneys, and the mucosa of the pelvis of the kindeys was congested. The mucosa of the intestines and urinary bladder showed hyperemia and ecchymosis. The cut surface of the liver oozed blood mixed with bubbles, and the mesentery was also congested with blood containing bubbles of gas. The meninges of the brain were congested and bubbles were seen in the superior longitudinal sinus, the sylvian arteries, and the Circle of Willis. In summary, this case exhibited massive gas formation within the whole vascular system.

Incomplete autopsies on the other 2 cases revealed marbling of the skin and frothy blood in the vessels of the skin and subcutaneous tissues. Particular attention was called to the finding of air bubbles in one case in the right carotid and brachial arteries. In attempting to explain the fact that some acute cases show extensive bubble formation and others do not, Schäffer pointed out that in some cases increased activity of the heart and lungs may rapidly get rid of the gas bubbles in the blood so that few or none may be present in death. Of a total of 135 fatal cases in compressed air work, Schäffer found 18 in which autopsies were available. Of these, 9 were completely negative as far as air emboli were concerned. With regard to the presence of air in the arteries, the only previous description, according to Schäffer, was that of von Wenusch (*1918*) 1896 who described air in the carotid arteries, the pulmonary arteries, and vessels of the portal system. In Schäffer's 3 cases, the characteristic findings were (a) capillary ecchymosis, (b) extravasation of blood into the thoracic and abdominal cavities, (c) skin emphysema, and (d) free gas in the body cavities. According to Schäffer, skin emphysema was described briefly by Pol and Watelle (*75*) 1854 and Heiberg (*1357*) 1878.

In a review of the morbid anatomy of caisson disease or diver's paralysis, Biggar in 1900 (*1355*), described intense congestion of the brain and cord as a nearly constant postmortem finding in all fatal cases of caisson disease. Microscopically, the cord revealed areas of softening, particularly in the lower dorsal region. The white matter was more often affected than the gray matter, and within the white matter the pathological process was found chiefly in the posterior columns and posterior portions of the lateral columns. Abdominal viscera were characteristically engorged with blood. In 1901, McKinlay (*1359*) described the case of a diver who died suddenly on reaching the surface. Air bubbles were present in the venous system and in the heart, and were particularly noticed in the Vein of Galen and in the choroid plexus. Brooks (*1356*) 1907 described the following characteristic pathological changes in caisson disease: (a) emphysema of the skin; (b) air bubbles in the heart chambers; (c) congestion of the lungs; (d) hemorrhages in the liver, spleen, and kidneys; (e) distention of the

bladder; and (f) areas of softening of the spinal cord. Reference was also made to lacerations within the brain tissue. A further case of an acute fatility in a diver was described by Rudge (*1362*) 1907 who reported air bubbles in body fats, the coronary veins, the auricles, the azygous veins, and joints.

In the case of a young caisson worker of 28 described by Oudard (*1361*) 1911, the victim had worked in the caisson at a depth of 17 m. for a period of 2 hours. Decompression lasted 10 minutes. Ten minutes after "locking out," he collapsed and died on the way to the hospital about 1 hour after decompression. Autopsy was not carried out until 64 hours after death, at which time air bubbles were reported in the right ventricle, in vessels of the stomach and great omentum, the femoral vein, the external iliac arteries and veins, the aorta, and the inferior vena cava. Minute bubbles could be expressed from the cut surface of the liver, and the lungs were emphysematous and congested. Bubbles were also present in the coronary vessels. The pia mater was markedly injected, especially in the Rolandic area and all vessels of the brain showed minute bubbles.

In summary, Oudard's case exhibited gas bubbles in both veins and arteries and in the left as well as the right side of the heart. In less acute cases, other workers have found gas bubbles only in the right ventricle. In such cases, bubbles have apparently not traversed the lesser circulation to reach the left heart and the systemic arteries. Oudard observed no macroscopic hemorrhages. For further descriptions of post-mortem findings in decompression sickness, reference may be made to Hill (*1083*) 1912.

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2. LESIONS OF THE CENTRAL NERVOUS SYSTEM

In 1870–71, Clark (*1373*) reported histories of 35 cases, some fatal, of workers brought to hospital from the caisson of the St. Louis and Illinois Bridge. In one worker of 30 who had worked for 2 hours in the caisson, there was severe pain in the lower extremities followed by paralysis of the legs, urinary bladder, and anal sphincter. The patient died 2 months and 11 days after the accident, and a post-mortem examination showed softening of the brain and cord substance. Pus was present in the cerebrospinal fluid, indicating a generalized infection of the central nervous system, masking the chronic manifestations of decompression sickness. In a caisson worker of 22 stricken with paralysis of the lower limbs, bladder, and sphincter, and dying 12 days later, there were congestion and softening of the brain and cord as well as of the abdominal viscera. The mucosal suface of the bladder was thickened and showed areas of ecchymosis. In a similar case, terminating fatally 5 days after the accident, there were congestion of the brain, cord, and meninges, and marked subarachnoid effusion. The spinal cord showed areas of softening in the lower dorsal region, and the veins of this part of the cord were thrombosed. The thoracic and abdominal viscera were highly congested. In a worker of 32, suffering from an acute attack of pain in

the arms and shoulders followed by paralysis of the lower limbs and dying 3 months and 6 days later, some softening of the brain was reported. In a case succumbing 2 days after the acute attack, a high degree of congestion of the brain and cord was observed. A case terminating fatally 12 days after the accident showed congestion of the brain and meninges, and softening of the cord in the lower dorsal region. Small clots of extravasated blood were seen on the external surface of the spinal cord. In all cases reported, the viscera were generally congested; and in many chronic cases, there were thickening of the bladder mucosa and extensive ulceration.

Since other studies indicate that the brain is usually spared in acute decompression sickness, the signs of softening in the cerebellum observed by Clark may be open to the question of whether post-mortem lesions complicated the picture. There seems no doubt, however, that acute softening does occur in the spinal cord, especially in the dorsal region as a result of sudden decompression from raised atmospheric pressures. Paul Bert demonstrated this experimentally in 1872 (*1366*) in a cat taken to 10 atmospheres and suddenly decompressed to normal atmospheric pressure through an accident to the apparatus. The cat was seized with convulsions and complete paraplegia. The animal was sacrificed the same evening, and showed a softening of the spinal cord particularly severe at the 11th and 12th dorsal levels. In 1878–79, Leyden (*1380*) reported a number of case histories of caisson workers with paralysis of the lower limbs, and urinary retention requiring catheterization in certain instances. One case in which post-mortem examination was performed 11 hours after death exhibited tears in the substance of the spinal cord. Such traumatic manifestations appear to be due to the mechanical effect of gas bubbles, and are an indication of the insult caused by sudden decompression. In contrast to this acute case of Leyden's, a report was given in 1880 by Schultze (*1390*) of a young caisson worker of 18 who was seized with paralysis of the lower limbs, as well as disturbance of bladder and colonic function. There was loss of sensation up to the level of the umbilicus. As a result of repeated catheterization, severe cystitis developed; there were decubitus ulcers. There was progressive loss of strength and the patient died 2½ months after the accident. White patches were present in the lower dorsal region of the spinal cord involving the posterior and lateral columns. The lesions were brittle and granular in character and appeared to take the form of a disseminated myelitis. Secondary ascending and descending degeneration was also present. In the gray matter of the dorsal region some nerve cells were degenerated; there was no evidence of tears in the substance of the cord. However, since 2½ months had elapsed between the accident and final termination in death, evidence of tears, had they existed, would have become obliterated.

A further contribution to the experimental pathology of decompression sickness was reported by Blanchard and Regnard (*1367*) in 1881. These investigators subjected dogs to raised atmospheric pressures followed by rapid decompression in a compression chamber in the physiological laboratory at the Sorbonne in Paris. Most animals succumbed a few minutes after leaving the chamber, while others survived for several days. In one case, the animal was paralyzed, and subsequently recovered almost completely. The particular dog was compressed to 7¼ atmospheres and subsequently decompressed in 15 seconds. Two and one-half minutes after being removed from the chamber the animal scratched its body violently as if there was great itching. At the end of 6½ minutes, while both limbs were paralyzed, the animal attempted to walk, dragging the hind quarter behind it. It was noted that the left hind leg was warmer than the right. On the next day, paralysis of the hind quarters was complete and 2 to 3 days later, urinary incontinence intervened. By the 16th day, the dog began to support its weight on the hind legs, and by the 18th day, it was walking much better. Urinary incontinence was nearly gone. By the 67th day, the animal was almost completely restored functionally, although a slight urinary incontinence remained. At this time the animal was sacrificed by pithing the medulla.

The spinal cord showed small hemorrhagic foci limited to the gray matter and the authors reported an acute parenchymatous myelitis. No sclerotic lesions were present anywhere in the spinal cord. The hemorrhagic areas were circumscribed and were seen in the posterior horn, the anterior horn or the region of the commissure. They were absent in the lumbar enlargement. In the white matter, the axis cylinders were hypertrophied and showed varicosities. Many had degenerated completely. The lesions in the white matter were of greatest intensity in the dorsal region of the spinal cord, and in this region were generally distributed throughout all parts of the white matter, but were mainly to be seen involving the lateral columns. In the upper one-fourth of the dorsal region of the cord, there was an area of extensive destruction of tissue in the posterior columns. In the dorsal region, the nerve cells of the gray matter were reported to have undergone considerable atrophy. Elsewhere the nerve cells of the gray matter appeared normal. This experimental case is of interest since it indicates a characteristic feature of the neurological manifestations of decompression sickness; namely, that excellent functional recovery is consistent with extensive, permanent cord lesions.

Pathological changes occurring in the spinal cord were also described in 1888 by Gowers (*1378*) as a disseminated myelitis. In commenting on the findings of Leyden and Schultze, Corning (*1374*) 1890 found the limitation of the spinal lesions to the dorsal portion of the cord difficult to explain on the basis of the gas bubble theory. As will be noted, Boycott and Damant (*1371*) 1908 explained the site of election of the characteristic lesions on the basis of the richness or poverty of the blood supply of the spinal cord. Hemorrhage within the cord in decompression sickness is apparently an unusual finding, but it has been referred to both by Boinet (*1369*) 1891 and Bassett-Smith (*1364*) 1892. Nikiforoff (*1385*) 1893 called attention to small cord hemorrhages in a caisson worker who died 48 hours after losing consciousness on "locking out." In this case, the tissues of the cord were seen to be separated apparently by gas bubbles, and many ganglion cells were compressed, vacuolated, or degenerated. The pathological changes reported were limited for the most part to the dorsal region of the spinal cord, and in the white matter there was swelling and vacuolation of the axis cylinders.

Acute punctate hemorrhages may have been responsible also for spinal lesions in the case of a diver presented by Sharples (*1392*) in 1894. This individual had been diving at a depth of 210 ft. for 2 weeks before the accident. On the day of the attack, the diver had made 4 dives. His ascent from the 5th dive was somewhat more rapid than usual, and when the helmet was removed at the surface, he complained of severe, sharp pains in the arms and legs, and then fell unconscious. He remained unconscious for 1½ hours, and on recovery complained of pains through both arms and into the fingers. The arms and legs were paralyzed, as were the bladder and rectum. Sensation was absent in the lower extremities. Two weeks later, there was cough with mucous rales, and dullness posteriorly in each lung. The subsequent clinical history followed a course characteristic of the subacute form of decompression sickness, with persistent urinary incontinence, cystitis, and large ulcerating bed sores. The patient became pyrexial and died, probably from sepsis, from large decubitus ulcers. Unfortunately, 36 hours elapsed after death before the cord was removed and fixed, and, therefore, there was extensive post-mortem autolysis. The white matter showed areas of softening in the cervical and other regions of the cord. The nerve fibers around these areas were swollen and the blood vessels were engorged. These broken-down patches were localized within the posterior and lateral columns. Throughout the cord, but particularly in the lower dorsal portion, areas giving the appearance of hemorrhage to the naked eye were seen. It appeared probable to Sharples that the original lesion was most extensive in the cervical region of the cord, an unusual finding, since most authors have described the site of election as being chiefly in the dorsal region. According to Drasche (*1376*) 1898, the spinal lesions in diver's paralysis arose from a disturbance of

nutrition of nerve structures as a result of obstruction of blood vessels by gas emboli. These bubbles produced their effect mainly in the dorsal region of the cord and particularly in the lateral columns. It was not certain, according to Drasche, whether the symptoms of diver's paralysis were to be ascribed to the effects of small areas of anemic necrosis with myelitis or to changes due to capillary tears.

In 1899, studies on the pathological anatomy of the spinal cord in decompression sickness were reported by Curcio (*1375*) and von Schrötter (*1388*). In 1900, Lépine (*1379*) decompressed rabbits and guinea pigs from a pressure of 10 atmospheres to normal pressure within a few seconds. Under these rigorous circumstances, hemorrhages and infarcts, as well as intense congestion, were found in the spinal cord. Lépine also stated the air bubbles were released in the central canal and in the interstices of the tissue.

Hemorrhages in the cord were reported by Engelbach (*1377*) in 1902, and Battaglia (*1365*) 1904 called attention to chromatolysis of the Nissal substance in the spinal cord. Lie (*1384*) 1904, in reviewing the work of Leyden, Schultze, and Nikiforoff, stated that Leyden believed that hemorrhages in the cord did not play a significant role. As previously mentioned, Schultze did not find extravasations of blood or tears in the tissue in a case dying 2½ months after the accident. It appears that Nikiforoff also did not attach importance to hemorrhage as a factor in the production of neurological symptoms. Lie reported the case of a diver of 49 years of age who had been diving for 15 years. On the day of the accident, he had made 3 dives at depths of 38 to 47 m. Death occurred 85 hours after the last dive. Punctate hemorrhages were seen on the cerebral hemispheres and the spinal cord was congested. Cut sections of the spinal cord examined by the naked eye showed multiple, minute hemorrhages and in the dorsal region there were small, clear flecks in the posterior columns and in the posterior part of the lateral columns. In many areas of the hemispheres, there were similar punctate hemorrhages, and clear foci were seen. In cases in which the insult is severe, Lie believed that the hemorrhagic manifestations were of significance as a cause of death, and it was the author's opinion that danger of such hemorrhages began at depths greater than 30 m.

A well-written, brief review of the pathological process in diver's paralysis was published in 1904 by von Schrötter (*1389*). Although the process was considered to be a myelitis by Leyden, Schultze, Van Rensselaer, Nikiforoff, and Sharples, von Schrötter believed that the lesions were due to ischemia of the tissue associated with liberation of gas bubbles, and that they were not inflammatory in origin. This view was previously expressed by Blanchard and Regnard (*1368*) 1881, and is confirmed by the best modern opinion available. von Schrötter called attention to Lépine's finding that only on sudden decompression from very high pressures (8 to 10 atmospheres) do tears in the tissue occur. von Schrötter reported the case of a diver who worked for 35 minutes at a depth of 48 m. On ascending to the surface, he fell unconscious after the helmet was removed, and subsequently developed paralysis of both legs with bladder and rectal disturbances. The case followed a typical clinical course with decubitus ulcers and terminated in death 40 days after the accident. Postmortem examination revealed multiple necrosis of the white matter of the spinal cord without evidence of hemorrhage. There was extensive glial reaction. In a second case, a diver of 5 years' experience worked for 30 minutes at 40 m. depth. After removal of the helmet, he was seized with excruciating pains in the back, followed 5 minutes later by complete paralysis of the upper and lower extremities. There was also paralysis of the bladder and colon, followed by decubitus ulcers. The patient succumbed 4 months after the original accident. Examination of the spinal cord showed ascending degeneration of the dorsal columns and the lateral cerebellar tracts. According to von Schrötter, the initial lesions in diver's paralysis consist of multiple areas of necrosis, particularly in the white matter, but to some extent in the gray matter. These lesions are mainly located in the dorsal

region of the cord, and they give rise to secondary degeneration.

White and Bainbridge (*1393*) in 1905 reported a case of fatal diver's paralysis in a diver of 38 years of age who was admitted to Guy's Hospital, London, on December 30, 1893, complaining of loss of power in the legs and sleeplessness. He had been a professional diver for 15 years, and had often noticed that he was unable to sleep after work. The author notes that many other divers have been troubled by insomnia to such an extent that they were forced to give up work for a time. The patient in question had had his first attack of paralysis of the legs 4 years previously as a result of a dive to a depth of 150 ft. At that time he was hopitalized for 3 months and discharged in good functional condition. The onset of the present attack was 12 weeks previous to admission, and followed a dive to a depth of 162 ft. As the diver emerged from the water, his hands and feet felt numb and tingling. Sleeplessness began to trouble him about 2 weeks later. On examination in hospital, there was foot drop, and the patient gave a history of gonorrhea and syphilis. Knee jerks and ankle jerks were normal, and plantar reflexes showed flexor responses on both sides. There was some weakness of the hands but no wasting of muscles. When the patient left the hospital on January 8, 1894, he could walk fairly well. He was readmitted on February 2, 1905, complaining of weakness of the legs and a cough. Three weeks previously, while working at a depth of 130 ft., he became entangled in a net and was submerged 1 hour and 20 minutes, and was then brought to the surface unconscious. On regaining consciousness, he complained of pain in the abdomen and on standing, there was weakness of the legs and a sensation of "needles and pins" in the palms and soles. The patient, himself, described his sensation as being raised off the ground and standing on holly. He remained in the hospital until his death 3 weeks later, when it was apparent that he had extensive pulmonary tuberculosis. The brain and cord, removed 24 hours later, showed no abnormalities on naked eye examination, and microscopic sections of the cord revealed no morbid changes in the white matter. In the gray matter of the lumbar region, the nerve cells appeared fewer than normal, especially the large motor neurones in the anterior horn. Some of the cells present showed evidence of slight necrosis. The perivascular lymph spaces in the lumbar region were larger than those in the thoracic or cervical regions. There was definite thickening of the small arteries in both gray and white matter, but no hemorrhages were seen. The author believed that the case was diver's paralysis and not of leuetic origin since there was recovery of function of the legs after each attack. The case is of interest in that the spinal cord presented a minimal pathological picture, both functionally and anatomically. It is thus apparent that the central nervous system possesses remarkable powers of recovery from the effects of decompression.

In 1906, von Leyden and Lazarus (*1382*), in a detailed report of myelitis, again referred to the cord lesions in caisson disease as a traumatic myelitis. The lesions, they believed, were due to tears in the cord substance caused by liberation of gas bubbles. Zografidi's report (*1394*) on decompression accidents in divers, published in 1907, should be consulted for further descriptions of case histories involving damage to the central nervous system. The report is based on 260 clinical observations with 7 autopsies, of which 2 were performed by the author himself. In one fulminating case, a diver of 40 years of age was decompressed suddenly after 20 minutes, working at a depth of 65 m. The victim was already dead when brought to the surface, and the body showed generalized emphysema. There were patches of capillary hemorrhage on the skin of the trunk and neck, and the conjunctivae were reddened and hemorrhagic. Zografidi described the typical clinical picture of the acute form of diver's paralysis with death within 2 to 3 weeks. In such cases, the diver has characteristically been immersed for several minutes to a depth of 40 to 70 m. He ascends rapidly and complains of intense pains in many parts of the body. There may be disturbances of hearing, loss of visual

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acuity, and paralysis, especially of the lower limbs. Consciousness may be lost for a few minutes, or an hour or more. The paralysis of the limbs may disappear after several hours and then return. Complete paraplegia may persist with anesthesia of the limbs and an area of painful hyperesthesia in the trunk, corresponding to the level of the cord lesion. There may be retention of urine and feces after 8 to 15 days of incontinence. The patient is often pyrexial, and decubitus ulcers may develop. The patient may die at this stage. If he survives, the muscles gradually become atrophic and contracted; reflexes are exaggerated and he walks with a spastic gait. Zografidi considered that the lesions in the cord were due to gas bubbles forming in minute cord vessels producing local patches of ischemia in the areas supplied by the occluded vessels. In intense fulminating cases, there might be hemorrhages within the cord. Zografidi considered that the pathological process was a true myelitis; he could not find evidence of bacterial infection. In one of Zografidi's cases, a diver, 30 years of age, was seized with intense pains and paraplegia of the lower limbs on ascending rapidly from 60 m. depth. The pain disappeared for 6 minutes and then returned permanently. The clinical course was characterized by fever, decubitus ulcers, incontinence, delirium, coma, and finally death 14 days after the accident. On post-mortem examination, the brain and spinal cord, as well as the meninges, were congested. No gas bubbles were seen in the dorsal region of the cord; generalized necrosis was observed, the blood vessels were dilated, and the axis cylinders were swollen or partly resorbed. There was some neuroglial reaction. In some sections, tears in the tissue could be observed. Secondary degeneration in the white columns was seen. Zografidi considered this a picture of transverse myelitis, with areas of necrosis and secondary degeneration above and below the region of myelitis. In another case of a young diver of 27, who died 4 days after a dive to 55 m., there were no necrotic areas in the spinal cord, but hemorrhagic foci were observed, as well as intense congestion. The author believed that early signs of myelitis were present.

For reports of a major study on the pathological changes in the spinal cord resulting from experimental decompression sickness, the reader should consult the papers of Boycott (*1370*) 1907–8 and Boycott and Damant (*1371*) 1908. Goats were exposed to 75 lb. gauge pressure for brief periods and decompressed rapidly. Bubbles were not found within tissue cells but were seen abundantly in the blood, bile, synovial, and amniotic fluid, and bubbles were also seen in fatty tissue. Bubbles were also present in the spinal cord, particularly in the white matter. In one experiment, a female goat was kept for 3 hours at the pressure of 75 lb. per sq. in., and then decompressed to normal in 58 seconds. The animal died in 12 minutes. Small hemorrhages were seen in the lateral columns of the cervical region of the cord and bubbles were found mainly in the antero-lateral columns. In another goat kept at 80 lb. pressure for 3 hours, breathing 36.6 percent oxygen mixture and then decompressed, air bubbles were found in the white matter close to the edge of the gray matter. Bubbles were not always found in the cords of animals dying shortly after decompression. It was found that air bubbles were about 5 times more abundant in the white matter than in the gray matter, bulk for bulk. In the gray matter, the bubbles were located mainly in the area close to the white matter, and the bubbles in the white matter were particularly abundant in the regions adjacent to the gray. Boycott and Damant believed that location of bubbles could be correlated with the local circulation, and they pointed out that the gray matter has a better circulation than the white matter and that the poorest circulation in the spinal cord is at the junction between the white and the gray matter. It is here, therefore, where most of the bubbles are located. It was found that there were about twice as many bubbles in the antero-lateral columns as in the posterior columns. Gas bubbles were most frequent in the dorsal and upper lumbar regions of the cord, and were least frequent in the lumbar enlargement. The authors found

no bubbles in the medulla, pons, or cerebral hemispheres. Many cases showed a definite relationship betwen the occurrence of bubbles and necrosis. The latter was ascribed to the blocking of the circulation by intravascular bubbles. Permanent paralysis which supervened in some of the experimental animals was attributed to softening of the spinal cord. This necrosis was confined to the central portions of the white matter, and there were no alterations in the periphery of the white matter or in the gray matter. No definite pathological changes could be demonstrated in Nissl preparations. The softening was particularly limited to the lower dorsal and upper lumbar levels of the cord.

Infarcts were seen only in white matter of the cord and in fatty tissue. The authors never observed them in abdominal viscera such as the spleen or kidneys. They presumed, therefore, that bubbles do not form effective emboli unless they increase in size *in situ* by accretion of fresh gas from their surroundings. It was believed that the sparing of the gray matter may be ascribed to its richer circulation. No softening was found above the level of the spinal cord. In two experiments, softening was present in the cord, although there was no lasting paralysis. The animals used in this series were exposed to pressures of 45 to 75 lb. per sq. in. for periods of 13 to 120 minutes. The decompression time was from one-half to 31 minutes, and the animals were sacrificed in 1 to 69 days. There was great individual variation in the susceptibility of the animals to the effects of decompression.

Cazamian (*1372*) in 1912 described a case of hematomyelia in a diver who had worked for 1½ hours at 30 m. depth. One hour after ascent, he lost consciousness for 50 minutes, and after recovery of consciousness was paralyzed in both legs. There was cyanosis of the face and violet marbling of the skin in various parts of the body, especially the abdomen and legs. The case did not come to autopsy. Sewall (*1391*) 1915 described the case of a sandhog of 42 years of age who worked for 1½ hours and locked out in three-quarters of an hour. Within a few minutes, there was weakness of the legs and by the following day, all motor impulses and reflexes below the umbilicus were lost. The patient died 6 months later with infected bed sores. In the lower thoracic region of the cord, there were areas of softening, with ascending and descending secondary degeneration. In a young worker of 20 who had been subjected for 45 minutes to a pressure of 49 lb. per sq. in. and had been decompressed in 28 minutes, there was weakness in both legs on leaving the lock. He returned to the medical lock for 12 hours, but a complete paralysis of the lower limbs supervened and death terminated the case 5 months later. There were areas of infarction in lungs and similar patches in both kidneys. The spinal cord showed softening in the lumbar and lower thoracic regions, and secondary degeneration was seen above and below the primary lesion.

Although pathological changes above the level of the spinal cord are unusual, they have been reported in the literature. Saraceni (*1387*) in 1923 described disturbances of the corpus striatum and Nordmann (*1386*) in 1928 observed edema, hemorrhage, and gliosis in the basal ganglia in decompression sickness.

For a recent historical study of the late lesions in caisson disease, the reader should consult the report of Lichtenstein and Zeitlin (*1383*) published in 1936. These authors described the history of a 63-year-old colored man who had suffered many attacks of the "bends" as a caisson worker. There was a history of paralysis of the bladder and the lower limbs, with partial recovery 25 years previously. Since that time, the patient had walked with a cane. The Kahn reaction was negative, as was also the spinal Wassermann reaction. The lower limbs were spastic, and knee and ankle jerks exaggerated. There was a positive Babinski sign. Abdominal and cremasteric reflexes were absent, and there was some difficulty of micturition. Post-mortem examination of the spinal cord revealed ascending and descending degeneration secondary to a severe destructive lesion of the thoracic portion. The white matter was more severely affected than the gray matter. Lichtenstein and Zeitlin believed that some bubbles formed within the blood stream in the cord, while others arose

outside of the circulation in the tissue and caused tears in the parenchyma of the cord. Except in very rapid decompression, the brain appeared to be immune to infarction because of its rich vascular supply. Moreover, within the spinal cord, the cervical enlargement was also rarely affected and this was attributed to its ample supply of blood from the anterior and posterior spinal arteries (vertebral system). The lumbar enlargement was infrequently affected, according to the authors, because of its supply by the *arteria spinalis magna* (from the spinal branch of the hypogastric artery). The thoracic portion of the cord is supplied with blood by small spinal branches of the intercostal and lumbar arteries (aortic system) and anastomatic twigs from vessels supplying the cervical and lumbar enlargement. This part of the cord has the least efficient circulation. The gray matter usually showed no pathological changes because of its larger vascular supply, and, according to the authors, because of the smaller amount of myelin. The central portion of the white matter is more profoundly affected than the peripheral portion, and this finding is in harmony with better blood supply to the periphery than the portion of the white matter adjacent to the gray matter. The pathological changes in the spinal cord are not those of a myelitis. The primary lesions are areas of softening produced, in the author's opinion, by obstruction of the circulation by gas emboli. These patches of myelomalacia may progress to the formation of glial scars, and these may be very numerous. Even permanent cord lesions in caisson disease are compatible with life and at least partially adequate functions.

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1365. Battaglia, M. Alterazioni traumatiche primitive della cellula nervosa. *Ann. Med. nav. colon.*, 1904, *2:* 701–709, pls. 1–4. [R]

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1377. Engelbach, P. Les accidents consécutifs au coup de pression. *Rev. méd. Normandie*, 1902, *3:* 57–63. [R]

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1381. Leyden, E. von and A. Goldscheider. Die Rückenmarksläsionen durch plötzliche Verminderung des Luftdrucks (Caissonlähmung). *Nothnagels spec. Path. Ther.*, (2. Aufl.) 1905, *10:* 143–147. [R]

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1384. Lie, H. P. Veränderungen in dem Nervensystem beim plötzlichen Übergang vom hohen zum normalen Barometerdruck. *Virchows Arch.*, 1904, *178:* 142–156. [Ch]

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1393. **White, W. H. and F. A. Bainbridge.** A case of diver's paralysis, with histological examination of the spinal cord. *Lancet*, 1905, *2:* 1101–1102. [Ch]

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3. EYE LESIONS

Although symptoms referable to the visual mechanism are sometimes encountered in decompression sickness, there are only a few references in the literature to actual pathological changes in eyes as a result of decompression from raised atmospheric pressures. Pick (*1401*) in 1907 surveyed the literature existing at the time and, from 1,000 cases of caisson disease, selected those in which disturbances of the eye were a feature of the clinical picture. These included 4 cases of transitory abducens nerve paralysis, one case of ptosis with weakness of accommodation, and one case of hemianopsia. Attention was called to 2 cases of temporary amaurosis. The first of these was a diver of 38 who dived to 48 m. depth and was submerged for one-fourth of an hour. The ascent from the bottom was accomplished within 2 minutes' time, and on reaching the surface, the victim was stricken with sudden blindness and motor asphasia. The second case was that of a 35-year-old diver who had made 6 dives in 1 day to a depth of 38 m. for 10-minute periods each. After the helmet was removed, on ascending from the seventh dive, the diver became unconscious. In 10 hours, asphasia developed and the patient could only distinguish between light and dark. In both of these cases, the condition was transient.

With one exception, ophthalmological lesions had not been previously observed, according to Pick, even in severe and fatal cases. The case alluded to was that of a German caisson worker who, on Nov. 15, 1906, worked in a caisson for 8 hours at a depth of 17 m. Ten minutes after "locking out," the worker was seized with severe pains in the body, motor weakness, and general fatigue. Pain and weakness increased during the succeeding days, and on the fifth day there was delirium and fever. On examination at that time, the temperature was 39.5° C., the pulse was 138 and respiration 44. There was Cheyne-Stokes breathing. A positive Babinski sign was present on both sides. Muscle and tendon reflexes were exaggerated and there was knee and ankle clonus. The bladder was distended and could be emptied only by catheterization. Lumbar puncture revealed nothing abnormal. The nerve head was reddened, and the retinal veins were dilated and dark. The retinal arteries were normal. The macular region was slightly edematous and swollen, and the fovea stood out as a contrasting dark red point. Around the macular area on both sides there were about 18 whitish retinal foci. These were opaque and homogeneous, with indefinite borders, and about 2 to 4 vessel diameters in size. They were located at the fine terminations of the retinal veins. In the right fundus there was a small round hemorrhagic area at the end of a vein. Twelve days after the accident the bilateral optic neuritis had regressed, and the retinal hemorrhage had disappeared. By the thirty-second day, the retinal appearances were normal. Pick suggested that the pathological changes in the retina were due to gas emboli lodging in both retinae at the communication between the capillaries and the fine veins. The author did not believe it surprising that the foci disappeared without leaving permanent traces, since similar foci due to other causes also disappear.

In 1907, Callan (*1396*) reported a case of double choked discs associated with compressed air illness. The patient was a young tunnel worker of 19 who had been working for 6 months in the East River tunnel, first as a lock tender and then in the caisson. For 2 months there was no trouble, but then he began to suffer slight attacks of the "bends" two to three times a week. One month previous to admission, he fell to the sidewalk shortly after leaving the lock. He was unable to stand because of weakness, and had to be helped home to bed. The next day, there was impaired vision and diplopia. The power in the legs was restored in a few days, but poor vision persisted. Also, there was double vision at times. Examination of the eyes showed slight convergent strabismus of the left eye, which was not constant. Mobility was good in the outside direction. Examination of the fundi showed choking of the discs on both sides with a few hemorrhages in the region of the nerve head and the macula. The disc on the right side was elevated 6 diopters, and on the left side 7 diopters. Both visual fields were concentrically contracted. The discs returned slowly to normal, but 3 months and 10 days after admission, the visual fields were still somewhat contracted.

Callan referred to a number of cases of caisson disease in which vision was affected. In only a few of these were the fundi examined, and these were found normal. Pol and Watelle (*75*) 1854 also reported blindness, some cases of which were permanent, but pathological reports are lacking. Oliver (see *1396*) reported cases in which patients complained of contracted visual fields and some of defective vision. In a few of these cases, the eye grounds were examined and found to be normal.

Callan's findings of choked discs are significant in indicating raised intracranial pressure as a possible factor in the clinical picture of decompression sickness. The pathological physiology of this elevation of intracranial tension is not clearly understood, and this is a point upon which fundamental research might well be undertaken.

In Callan's case, there was presumably complete recovery of the optic nerve. That this may not always be so is indicated by a report on partial optic atrophy in a caisson worker published by Genet (*1398*) in 1933. The patient in question was a 27-year-old caisson worker at Neuville-sur-Saone. Four hours after leaving the caisson, he suffered violent pains in the right eye, the right side of the head, and the right knee. Twenty-one days later, vision in the right eye was found to be diminished, and on examination of the right fundus 1¼ years later, the nerve head was found to be pale and the retinal arteries and veins diminished in size. No hemorrhage was seen and there was no change in the visual fields. The pupils were equal, and reaction to light and accommodation in the left eye showed no abnormalities. The author believed that this partial optic atrophy might have been caused by gas emboli in the optic nerve.

Genet referred to a report of subconjunctival ecchymosis in a diver, and similar findings in caisson workers have been reported by Barrat and Bastian (*1395*) 1936 who called attention to dimming of vision, conjunctival hyperemia, and ulceration of the cornea.

1395. Barrat, [ ] and [ ] Bastian. À propos d'une affection oculaire rencontrée chez des ouvriers travaillant dans des caissons sous-marins. *Arch. Méd. Pharm. nav.*, 1936, *126:* 273–305. [Ch]

1396. Callan, L. W. Double choked disks associated with compressed-air disease (caisson disease). *Arch. Ophthal., N. Y.*, 1907, *36:* 509–512. [Ch]

1397. Carson, L. D. Ocular effects of altitude flying and of deep sea diving. *Arch. Ophthal., Chicago*, 1945, *33:* 173–176. [M, R]

1398. Genet, L. Atrophie optique partielle et maladies des caissons. *Bull. Soc. franç. Ophtal.*, 1933, *45:* 318–321. [Ch]

1399. Genet, L. Atrophie optique partielle et maladies des caissons. *Lyon méd.*, 1933, *151:* 575–577.

1400. Pflimlin, R. Beteiligung des Auges bei der Caissonkrankheit, insbesondere Kataraktbildung. *Klin. Mbl. Augenheilk.*, 1934, *92:* 54–58. [Ch]

1401. Pick, [ ]. Augen-Erkrankungen bei Caisson-Arbeitern. *Zbl. prakt. Augenheilk.*, 1907, *31:* 169–172. [Ch]

4. EAR LESIONS

Vertigo, pain, disturbances of hearing, and other symptoms referable to the middle and inner ear may be included in the clinical

picture of decompression sickness. It appears quite clear that trauma can be inflicted upon the middle and internal ear of caisson and tunnel workers and divers, not only during compression, but also during and after decompression. In the first group, that is to say, those affected by compression, the symptoms may be temporary or permanent. In the second group, the disturbance is more usually persistent. Although both the cochlear and vestibular portions of the inner ear may be affected in decompression sickness, analysis of case histories indicates that the cochlear portion of the labyrinth is slower to recover than the vestibular portion.

During compression, the traumatizing factor is failure of equalization of pressure in the middle ear. This failure of entry of air through the Eustachian tube into the middle ear during compression not only affects the middle ear, but may also result in vascular stasis and hemorrhage in the inner ear. In decompression, the aural lesions may have their origin in bubbles of gas forming in the inner ear and producing areas of necrosis. The effect of rapid decompression upon the ear has been examined experimentally by Vail (*1408*) 1929 who took a rabbit to a pressure of 70 lb. in 1½ minutes. The animal remained at this pressure for 1 minute, and was then decompressed within 3 minutes to 30 lb. One and one-half minutes later, decompression to 10 lb. was carried out and one-half minute later the chamber was returned to normal pressure. Two other rabbits and one dog were taken to 75 lb. within 1 minute's time, and kept at that pressure for 1 minute and then decompressed to sea-level within 3 minutes. All aural lesions in these animals were apparently the same. There was copious hemorrhage in the middle ear, apparently from small vessels in the submucosa, since the mucosa was lifted off its bony bed. In one case, the hemorrhage had penetrated into the vestibule, where it filled the cavity almost entirely. The structure of the inner ear, mastoid cells, and temporal bone marrow was little altered.

Otani (*1407*) 1930–31 examined the pathology of the auditory organs in experimentally produced decompression sickness in rabbits. There was hemorrhage and leucocytic infiltration in the tympanic mucosa. Blood was present in the middle ear. The endolymphatic and perilymphatic channels of the cochlea and semicircular canals were swollen, and the cells of the organ of Corti were involved. There was also lymphocytic infiltration in the subepithelial tissue of the cristae acusticae and mononuclear and polymorphonuclear leucocytes were found in the region of the cochlear and vestibular nerves. In histological preparations, evidences of large numbers of air bubbles in the blood vessels of the auditory passages were seen.

For a review of disturbances of the ear produced by compression and decompression, the reader should consult a report by Lestienne (*1404*) published in 1933. He reviewed early references on the effect of compression on hearing. Lestienne described the case of a caisson worker at Suresnes who was stricken with vertigo and deafness in the right ear one-half hour after exit from a caisson. Recovery was complete in 3 days. In another case of a worker of 30 years of age who was decompressed rapidly after working for several hours at a depth of 25 m. there was ringing in the left ear with deafness, but no vertigo or vomiting. Twenty days later, audition was normal in the right ear, but there was apparently total destruction of the left cochlea, with functional integrity of the vestibular apparatus. A worker of 32 years of age, who had worked for 7 hours at a depth of 24 m. was decompressed in 35 minutes. Twenty minutes later, there was rotatory vertigo with vomiting, and deafness on both sides. For 8 days the patient complained of incessant noises in both ears, and after 4 days, hearing began to return in the right ear. Two days later, audition in the left ear began to return. Seven months later, the condition had become stationary; the patient experienced slight vertigo at times and very slight pounding in the ears. In typical cases of aural involvement in decompression sickness, there is vertigo and pounding in the ears. There is sometimes unilateral deafness, and occasionally such symptoms as cold sweats, vomiting, and pallor. Usually, the patient

takes to his bed for 2 to 8 days, and there is persistent headache for some days. In favorable cases, auditory and labyrinthine symptoms are rapidly relieved and progress to complete or nearly complete recovery. In a second group, the patient is left with persistent lesions of the organs of hearing and equilibrium. In these cases, according to Lestienne, there is always hemorrhage of the internal ear. Lestienne called attention to lesions in the internal ear investigated by earlier workers. In one such patient, dying after being subjected to compressed air, small clots and perivascular exudates were seen in the vessels of the labyrinth. Otherwise the vessels were empty of blood. The cochlea was detached at various points. In the nerves themselves and in the spiral ganglion, no blood was seen. Hemorrhages were observed in the anterior and lateral portions of the scala tympani, and blood was also seen at several points in the scala vestibuli. The vestibule was almost always empty of blood, but blood was seen in the membranous and osseous portions of the semicircular canals. Although these lesions have been ascribed to gas emboli, Lestienne believed that hemorrhagic lesions could result only from the mechanical action of pressure changes in the middle ear. Regarding prognosis in inner ear lesions, Lestienne considered that complete recovery may take place if there is simply hyperemia with exudation. Where hemorrhage has occurred, the prognosis must be more guarded, and one may expect persistent equilibratory disturbances and partial or total deafness. For further studies on pathological lesions in the ear resulting from changes in air pressure, the reader may consult reports by Malan (*1406*) 1933, Magnotti (*1405*) 1936, and Chiappe (*1402*) 1939.

1402. Chiappe, E. Lesioni dell'orecchio interno da decompressione. (Rilievi istopatologici). *Oto-rino-laring. ital.*, 1939, *9:* 149–178.

1403. Cipollone, L. T. Sopra alcune alterazioni che possono determinarsi nell'organo dell'udito per azione dell'aria compressa. Nota di patologia sperimentale. *Ann. Med. nav. colon.*, 1911, *2:* 159–185. [P]

1404. Lestienne, J. Des accidents labyrinthiques chez les ouvriers de chantiers de travaux a l'air comprimé. Maladie des caissons. *Ann. Oto-laryng.*, 1933, *1:* 200–217. [R]

1405. Magnotti, T. Alterazioni del naso, laringe ed orecchio in animali sottoposti a compressione e decompressione di aria (aviatori e lavoratori dei cassoni). *Oto-rino-laring. ital.*, 1936, *6:* 235–251.

1406. Malan, E. Traumatismo sonoro acuto sperimentale. *Valsalva*, 1933, *9:* 465–466.

1407. Otani, N. Beitrag zur Caisson-Krankheit. (Zur Pathologie des Gehörorgans bei der experimentell erzeugten Caisson-Krankheit.) III. *Zbl. Hals-, Nas.-u. Ohrenheilk.*, 1930–31, *16:* 460. [P, R]

1408. Vail, H. H. Traumatic conditions of the ear in workers in an atmosphere of compressed air. *Arch. Otolaryng., Chicago*, 1929, *10:* 113–126. [P]

1409. Vail, H. H. Traumatic ear conditions in workers under compressed air. *Trans. Amer. otol. Soc.*, 1929, *19:* 139–166.

5. BONE AND JOINT LESIONS

The first suggestion that caisson disease might be responsible for bone and joint lesions was made by Twynam (*1436*) in 1888. This investigator described a caisson worker who suffered from pain and swelling above the right knee leading, 2 months later, to abscess formation and drainage. A draining sinus persisted for 2 years, at which time an amputation was performed through the lower third of the femur. The shaft of the bone was found to be necrotic, and it was suggested that the primary lesion had been necrosis of the shaft of the femur, with secondary infection.

In 1907, Jacobj (*1424*) described the mechanical effects of decompression on bones and joints. Detailed case histories of caisson workers suffering from chronic joint disturbances were given by Bornstein and Plate (*1415*) in 1911–12. In 1909, Bornstein (*1414*) observed 2 cases of emphysematous swelling in the subcutaneous fat of the lower extremities in "bends." This indicated, according to Bornstein, a relationship between peripheral bubble formation and the "bends." Another argument for the peripheral origin of "bends" pain, according to Bornstein, was the beneficial effect of local massage. The question of exactly where the bubbles form—within the muscles, local fatty tissue, in peripheral nerves or in the bones—was discussed by Bornstein and Plate. Their experience with decompression sickness was based on approximately 500 cases of the "bends" encountered during the building of the Elbe Tunnel at Hamburg. Nine of

these cases, showing chronic changes in the skeletal system, were reported in detail. In 1 of these cases, that of a young caisson worker of 28 who had been working under a pressure of 3 atmospheres (absolute) for 2 months, pains developed in the right hip and knee. These persisted for over a year and a half. At the end of this time, there was painful limitation of movement of the right hip, and X-rays showed irregularity of the head of the femur which contained focal areas of increased opacity corresponding to the irregularities of the surface of the head of the femur. In a second case, an engineer of 28 years of age who had been subjected to raised atmospheric pressure in a caisson operation at a depth of 23 m., roentgenograms showed irregularities of the head of the humerus with a focal area of decreased density in the upper part. There was some symptomatic improvement after 8 weeks of physical therapy, but no change in the X-ray picture was seen. In a third case, that of an engineer of 36, who had been subjected to raised atmospheric pressures intermittently over a period of several years, and who had suffered from "bends" pains in the arms and legs, there was X-ray evidence of distortion of the heads of both femurs with irregular foci of diminished density in the bone. Bornstein and Plate concluded that a chronic arthritis may result as a sequel of caisson disease. It was suggested that gas bubble formation might lead to a disturbance of nutrition in circumscribed areas of bone. This primary focal disturbance of the bone might then lead to a malfunction of the joint. A regression of the condition was observed in some of the author's cases, and even in serious conditions of the joints improvement was not excluded. The heads of the femur and humerus were sites of election, and this was considered to be due to the fact that the blood supply was poorest in these regions and conditions were, therefore, more favorable for the formation of emboli. These cases were also discussed by Plate (*1429*) in 1912.

Bassoe (*1412*, *1413*) in 1912 and 1913 reported case histories illustrating late bone and joint manifestations of compressed air disease. His later paper (*1413*) is particularly recommended for good descriptions of case histories. Of 161 cases, 87 complained of ear affections and in 65 of these there was permanent impairment of hearing. One hundred and forty-five gave a history of "bends," and in 34 cases there was paralysis. This was generally transient, but in 3 workers there was permanent paralysis of one arm and in 3 other cases both legs were permanently paralyzed. There were 11 cases of chronic joint pain and stiffness, and one case showed X-ray evidence of arthritis deformans. Twelve cases presented signs of some degree of permanent cord disease. There seemed, according to Bassoe, to be a definite etiologic relationship between acute attacks of arthralgia, or "bends," and subsequent chronic arthritis in the absence of spinal lesions. In addition, there were cases with signs of trophic osteoarthropathies dependent, according to Bassoe, on cord lesions. In one of Bassoe's cases, a worker of 40 years of age, there had been a spontaneous fracture of the patella, and 2 years later a fracture of the external tuberosity of the humerus. Signs of cord disease were present. In a caisson worker of 46 years of age, who had suffered from repeated attacks of the bends for 27 years, and who had had one episode of disturbance of bladder function with incontinence, roentgenograms showed islands of atrophy and sclerosis in the tibia.

One of Plate's cases (*1430*), reported in 1928, was a caisson worker in a German tunnel operation. In 1908, he had suffered a generalized attack of pain, especially severe in the left hip joint, after leaving work. On X-ray examination in 1926, there was deformity of the head of the left femur, reduction of the joint space, and a generalized picture described by the author as that of arthropathia deformans. The condition was not associated with a change in blood sedimentation rate, and was not, therefore, considered by Plate to be an inflammatory, but rather a regressive process.

Chronic joint changes in caisson workers were described in 1934 by Christ (*1416*) in the building of the Krembser Kraftwerk below Basel. In this project, the caisson operated for 4 years at pressures of 2 to 2½ atmospheres. No acute severe manifestations of caisson dis-

ease were seen, and particularly there were no spinal cord disturbances. However, in four workers there were resorption foci in the head of the femur. In every one of these cases, the patient had worked for a long time in the caisson. Each case was characterized by pain and limitation of movement. Christ believed that a single exposure to "high air" was insufficient to produce chronic bone and joint changes. The primary disturbance, he believed, was in the bones themselves, whereas the accompanying arthritis was considered secondary. X-ray pictures were given showing areas of decalcification. In a 37-year-old man, who had worked in caissons for 5 years, and who had been subjected to pressure daily for the previous 3 years, a history was given of two earlier attacks of acute caisson disease. Some weeks before reporting he had complained of pain in the left hip, a limp, and painful restriction of movement. The X-rays showed multiple areas of decalcification.

ray evidence of chronic hip-joint lesions in divers was reported by Seifert (*1432*) in 1936.

In 1937, Jaeger (*1425*) described the history of a patient subjected to high pressure 5 years previously. There was no official history of an acute attack of caisson disease, but the patient had complained on one occasion of pain in the left hip and leg. Within 3 weeks, the acute symptoms had subsided, leaving a gradually developing chronic arthritis. There were subsequent attacks of acute pain on leaving caisson operations, and when the patient was seen, X-rays showed flattening and broadening of the head of the left femur, reduction in the size of the joint cavity, changes in the wall of the joint capsule, and numerous clear areas in the head of the femur between irregular lines of thickening. This picture of arthritis deformans became more accentuated in the course of the following year. Jaeger believed that the joint damage was not causally related to a single accident, that usually chronic joint disturbances supervened only after many attacks of caisson disease.

A brief report of bony changes in caisson disease was given by Frank and Knoflach (*1420*) in 1938. In this case—that of a worker of 39 years of age who had worked in caissons for 18 years—the patient was hospitalized 4 years previously after a rapid decompression from the caisson. There was loss of sensation and motor power in the right upper arm, and pain on movement in the right shoulder and hip joints. These symptoms subsided in 14 days, but pain in the right hip joint persisted. Two years later, the patient visited the hospital because of pains and limitation of movement in the right hip and shoulder. X-rays of the right hip joint showed round flecks of diminished intensity in the head of the femur. The joint was intact. In the head of the humerus, there were fissures about 1 mm. wide in the bone. These necrotic foci in the bone are due, according to Frank and Knoflach, to liberation of bubbles within the osseous tissue. This is particularly likely to occur in arteries with few anastomoses.

Chronic osteoarthrosis in caisson disease was referred to by Barbara and Isola (*1411*) in 1939.

A significant modern report on the pathology of bones and joints in caisson disease is that of Kahlstrom, Burton, and Phemister (*1427*) published in 1939. In one case, there was necrosis of the epiphyses, with secondary deforming arthritis and massive necrosis of the shafts of the long bones in caisson disease of 35 years' standing. Roentgenograms of the hip joints showed flattening of the femoral heads, with narrowing of the joint spaces and marginal lipping. Scattered areas of reduced density were seen in the subarticular portions of the femoral heads and the acetabula, interspersed with areas of increased density. X-rays of the lower three-fourths of the femur revealed an oblong area of altered density in the medullary region surrounded by an area of increased density. In the right femur, there was a similar area consisting of a central necrotic area in the shaft with a calcified and ossified zone of demarcation. Changes were also seen in the left shoulder joint and the left tibia. When this case came to autopsy, post-mortem examination showed lumbar scoliosis and central necrotic areas in the diaphysis of the humerus. There was a deforming arthritis in the humeral head and loose bodies in the shoulder joint. In both femurs, the head of the bone was deformed and remnants of infarcts were

seen in the lower half of the diaphysis. A calcified necrotic area was seen in the external condyle of the right femur. Microscopic examination showed deforming arthritis in the joint and central necrosis in the shaft of the bone with calcification in the periphery of the lesion.

In general, the findings suggested to the authors a multiple infarction in the long bones resulting from presence of gas bubbles. The changes in these necrotic areas varied according to the location and duration of the involvement. In necrotic areas bordering on the joint, there was a varying amount of collapse due to weight-bearing with replacement by new bone together with calcification of non-substituted portions. The articular cartilage overlying the involved areas breaks down and is replaced by fibro-cartilage, and thus a more or less extensive arthritis deformans becomes established. The prevailing theory is that the arthritis deformans is secondary to vascular blockage and necrosis of bone underlying the articular cartilage. When the necrotic bone is situated in the diaphysis or in the epiphysis away from the arthritic surfaces, collapse did not occur and there was some evidence of invasion and replacement by new bone. The authors raised the question of whether the necrosis was produced by gas bubbles in the blood obstructing end arteries, or by direct pressure on blood vessels and other tissues after liberation from fat outside the vascular system. Since the bones involved are those rich in fat, it seemed that the theory of direct pressure was a likely one; however, involvement of the diaphysis in some cases without lesions in the epiphysis and *vice versa* are points in favor of infarctions produced by gas bubbles, or some other form of intravascular obstruction.

For other cases of caisson disease with special reference to bones and joints, the reader may consult the report of Coley and Moore (*1418*) published in 1940 and a paper by Gordon and Heacock (*1422*) 1940. In the latter report, a worker suffered a fracture of both tibias while working under a pressure of 25 lb. X-rays showed gas in the synovial sac in both knee joints, and there was crepitus around the knees.

An important contribution to our knowledge of roentgenographic findings in caisson disease of bone is that of Rendich and Harrington (*1431*) published in 1940. Four cases are reported in detail. The bony involvement included aseptic necrosis in the hips, shoulders, and knees, medullary calcification in the diaphyses of the long bones and hypertrophic arthritis. X-ray evidence of aseptic necrosis in the tibia and femur confirmed by biopsy findings was reported by Walker (*1437*) in 1940.

An excellent review article dealing with the bone and joint lesions in caisson disease was published in 1941 by Mouchet and Mouchet (*1428*). The reader should also refer to an article by Herzmark (*1423*), published in 1942, for a review of chronic changes in the bones as a result of caisson disease. Herzmark believed that the bony lesions result from obstruction of vessels by gas emboli, or pressure against blood vessels by gas bubbles. Infarction and aseptic necrosis of varying extent result, and this is followed by attempts at repair. If necrosis occurs at a weight-bearing surface, collapse and deformity may supervene. It is stated by Herzmark that the bones are selectively affected because the fat of the bone marrow has a high affinity for nitrogen. The heads of humerus and femur are the most frequently involved areas.

It is difficult to say how severe the initial attack must be before pathological changes appear in the bones. Coley and Moore believe that lesions in bones or joints may follow even a single attack of caisson disease, provided it is of sufficient intensity. Regarding the length of time which must elapse between the acute attack or attacks and the appearance of pathological changes in the bones or joints, no exact data are at present available. It does appear, however, that at least several months must elapse between the acute attack and the earliest recognizable changes on X-ray examination. In many cases, no clinical symptoms referable to the joints or bones are observed until flattening and distortion of the heads of the long bones cause arthritis. Permanent disability of one or more joints may then

rapidly supervene. This sudden onset of the condition may be explained, according to Herzmark, by the fact that the cortex of the head of a bone, thinned by aseptic necrosis, suddenly gives way as a result of some minor injury. Herzmark points out that acute attacks may or may not be related to chronic bone and joint changes, and that treatment of acute attacks by recompression may lead to a remission of the acute symptoms, but may not prevent the late changes. In a case reported by Herzmark, a caisson worker with 6 years' experience and a history of several mild attacks of the "bends," was struck on the shoulder by a piece of muck and three weeks later on the back of the head by a pipe. Subsequently, there was pain in the hips and legs, and on X-ray examination, the shoulder and hip showed aseptic necrosis, fragmentation and flattening of the heads of the bones. The lesions were in the spongy bone and did not extend into the joints. Flattening of the head of the bone, in this case, was due to destruction of bony tissue beneath the articular surface with collapse of the articular surface into the underlying tissue. Less extensive fibrocytic changes were observed in the lower half of each femur.

A detailed case of caisson disease of the bone was reported by Swain (*1433*) in 1942. This patient was a man of 37 who had worked in compressed air for 4 years and had suffered repeated attacks of mild "bends." This case came to autopsy, and bone lesions were carefully studied. Swain stated that the nonarticular lesions in the shafts of the long bones are usually symptomless. These shaft lesions consist of medullary infarcts appearing as central areas of dead bone, with irregular, thickened outlines due to replacement by new bone at the periphery of infarcted areas. Small infarcts may become completely calcified. The articular lesions, according to Swain, are commonly bilateral and affect the hip and shoulder joints preponderantly. He agrees with other authors in concluding that the primary lesions consist of foci of aseptic necrosis in cancellous portions of the bone, which devitalizes the overlying articular cartilage. With weight-bearing and continued work, the articular surface collapses. Loose bodies may form in the joints and painful symptoms develop. Swain believes that the condition is produced by the presence of gas bubbles in or around nutrient blood vessels. Whether or not necrosis is due to intravascular or extravascular pressure by gas bubbles is uncertain. The experiments of Kahlstrom, Burton, and Phemister, who failed to produce bony necrosis in dogs by injecting air into the femoral arteries, suggested the possibility to these authors that the bone lesions in caisson disease were due to gas liberated in the medullary cavity under sufficient pressure to asphyxiate the tissue rather than to intravascular emboli. Swain pointed out that external trauma determined the site of the symptomatic lesions in some cases and that injuries associated with weight-bearing and heavy labor added to the destruction of the articular surfaces, if the underlying bone was rendered avascular by infarction. Aseptic necrosis of bone of undetermined etiology does occur, but is apparently rare.

In 1943, there appeared a report on caisson disease of bone by Allan (*1410*). This paper contains a useful survey of the findings of previous workers and should be consulted. The X-ray findings are described and the pathological picture carefully outlined. The differential diagnosis from chronic sclerosing osteitis, low-grade sclerosing, osteogenic sarcoma, calcifying enchondroma, bone syphilis, and tubercular osteomyelitis is discussed.

The reader's attention is directed to a report of a series of 50 patients with bone lesions by Taylor (*1434*) in 1943. Of these patients, 39 were males and 11 females. Eleven of the males gave a history of continued exposure to high atmospheric pressures. In 1 patient, there was but a single exposure. Joint and shaft lesions were present in the 12 individuals who had worked under compressed air for varying periods of time. Some had had the "bends" or other symptoms of decompression sickness, while others had not. Taylor emphasized that shaft and joint lesions did not develop immediately after decompression sickness, but that some time must elapse. He also stated that the shaft lesions are usually asymptomatic and accidentally discovered. In agreement with

other authors, he considered the joint lesions secondary to underlying bony changes. Shaft lesions were present in some patients and joint lesions in others, while some presented both types of lesions. These same characteristic lesions were found in 38 individuals who had never worked in compressed air, and in these, no etiological factor is apparent. The bone lesions are reported by Taylor to be single or multiple and are often bilateral. In the caisson workers, the lesions were more often extensive and multiple than otherwise. In the non-caisson workers where the lesion was single and not extensive, the reparative changes were usually greater. Taylor was unable to find any record in the literature of divers or aviation personnel with bone changes following aero-embolism.

For a recent review of caisson disease of bones, the reader should consult Comroe's book on arthritis and allied conditions (*1419*) published in 1944. In summary, it may be stated that the primary lesion in caisson disease of bones consists of a massive aseptic necrosis. Involvement of the articular cortex leads to the slow development of a deforming arthritis with or without osteocartelagenous loose bodies. Aseptic necrosis results apparently from interference with bone nutrition by emboli in the main nutrient vessels or from pressure on the vessels due to bubbles. This leads to absorption of bone, collapse, and to some extent, new bone formation in or near the epiphysis. Characteristic changes also occur in the diaphysis of the bone. X-rays show a multiple distribution of infarcts in the medullary bone, while cortical changes are rare.

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IV. COMPRESSED AIR INTOXICATION

Men exposed to increased air pressure of 4 atmospheres (absolute) or above are euphoric, confused, and may show neuromuscular incoordination. Individual variations in susceptibility to these effects exist and this has been attributed by some authorities in part to differences in emotional stability. The picture exhibited is strikingly similar to that seen in alcoholic intoxication and is approximately as variable. At high pressure—10 or 11 atmospheres (absolute)—even the most stable persons are so intoxicated that clear thought and efficient performance are impossible.

The cause of this slowing has been variously attributed to: (a) the stimulating effect of the increased tension of oxygen, (b) the narcotic effect of the increased tension of nitrogen, (c) the pressure effect alone, and (d) a purely psychological effect.

Both Phillips (*37*) 1931–32 and Hill and Phillips (*32*) 1932 stated that the psychological changes encountered in deep diving are due to purely mental—not physical—causes. They described several cases of failure of accomplishment under pressure which they demonstrated by psychological methods to be due to claustrophobia.

Behnke, Thomson, and Motley (*1439*) 1935 ascribed these psychological changes to the narcotic effect of the increased nitrogen tension. Their experiments were carried out at a temperature of 25° C. and 50 percent humidity, and their nine subjects were exposed to a pressure of 4 atmospheres (absolute) for 1.5 to 5 hours (including decompression time) in a dry pressure chamber. There was a feeling of stimulation, assurance, and well-being as maximum pressure was approached, and subjects showed a tendency toward laughter and loquacity. Responses to visual, auditory, olfactory, and tactile stimulae were delayed. There was loss of power of association and a tendency toward fixation of ideas. Subjects made mistakes in arithmetic and in recording figures. There was loss in fine neuromuscular control and coordination. This impairment could be controlled and compensated for by slower movements. In one test carried out at 10 atmospheres (absolute), the subject complained of numbness and was unable to take a pulse reading. Behnke, Thomson, and Motley stated that the changes noted are similar to those caused by agents such as alcohol and ether which depress the higher nerve centers. Breathing pure oxygen at one or more atmospheres does not produce similar effects. The authors believed that the symptoms were due to the narcotic action of nitrogen gas, which is taken up by the central nervous system according to the Meyer-Overton law.

Behnke and Yarbrough (*2495*) 1939 found that the symptoms disappeared when helium was substituted for nitrogen. Argon was found to have a greater narcotic action than nitrogen.

Haldane (*1441*) 1941 estimated that at a pressure of 20 atmospheres or more, the density of a helium-hydrogen mixture would be such as to exert narcotic effects. Lawrence and coworkers (unpublished) found that preanesthetic symptoms occurred in a subject breathing an oxygen-krypton mixture at atmospheric pressure.

In the rescue and salvage operations on the *Squalus*, Behnke and Willmon (*1440*) 1939 found that many experienced divers diving to 240 ft. on air had to terminate dives because of symptoms of narcosis. On shifting to helium-oxygen mixtures, the symptoms were abolished. The symptoms of nitrogen narcosis were found to vary to some extent with the individual and the efficiency of performance

of subjects suffering from nitrogen narcosis showed considerable individual variation.

Shilling and Willgrube (*1443*) 1937 made a quantitative study of the mental and neuromuscular reactions associated with high pressures. Human subjects were exposed to pressures of 6 atmospheres (absolute) or more and their performance on arithmetic and number cross-out tests, as well as their reaction time, were studied quantitatively. The subjects were 46 officers and men attached to the deep-sea diving school. These personnel were subjected to pressure in a compressed air chamber which simulated wet dives. Progress from a simulated depth of 100 ft. to 300 ft. was marked by greatly increased time differences required to complete the arithmetic problems. At 300 ft. equivalent, the increase in mean time was 31.42 seconds, while at 100 ft., it was 6.89 seconds. The actual mean time of accomplishment of the problems at 1 atmosphere was 59.54 seconds (standard deviation 21.55 seconds). The slowing effect on mental activity was less in an experienced group of divers than in inexperienced personnel. The number of mistakes in calculation under pressure was also adversely affected, and there was, in addition, a steady loss in the performance of the number cross-out tests. The light-to-touch reaction time was also slightly but noticeably affected. The essential difficulty appears to be slowing of cerebral function, and it was found that men with high mental ability do not fail as quickly as those who are less intelligent.

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V. OXYGEN INTOXICATION

A. GENERAL STUDIES ON OXYGEN POISONING

No investigation of the literature on the toxic effects of oxygen would be complete without reference to the classical work of Paul Bert (*16*) 1878. For a modern, complete, and authoritative review of the subject, the reader will find an article by Bean (*1445*) 1945 extremely helpful. Frequent reference has been made to this review in organizing the literature on oxygen poisoning, and in preparing the comments which follow. The reader will note that discussion of the neuromuscular and subjective reactions to compressed air are considered in another section, (p 162), and for further work on the relation of oxygen to submarine and compressed air medicine, reference should be made to the section on oxygen administration, (p. 278).

As Hederer and André (*1448*) 1940 have pointed out, two principal manifestations of oxygen poisoning may be distinguished. The first is the so-called "Paul Bert effect" consisting of epileptiform convulsions at high oxygen pressures. The second manifestation is the so-called "Lorrain Smith effect," or subacute poisoning, consisting of an irritation of the pulmonary alveoli, and developing under oxygen tensions of about 0.7 to 0.8 atmospheres of oxygen.

Although the pulmonary manifestations are characteristically observed at relatively lower oxygen tensions, while the convulsive seizures are characteristic of high oxygen pressures, nevertheless, the lungs may also be involved at very high pressures of oxygen. Hederer and André (*1448*) called attention to the fact that the toxicity of oxygen depends not only upon pressure, but also upon the duration of action. Hypothermia was stated to be symptomatic of acute, as well as subacute, oxygen poisoning. Oxygen tolerance of young animals was greater than that of older individuals, and fasting raises the level of tolerance. The addi-

tion of 5 to 7 percent carbon dioxide to the inspired oxygen tended to lower the threshold and to precipitate oxygen convulsions. The convulsive manifestations were stated to be aggravated by strychnine. Barbiturates retard, attenuate, or even prevent, the convulsive seizures. For further studies on the general aspects of oxygen poisoning, reference may be made to reports by Hansen (*1447*) 1925; Holste (*1449*) 1938; Binet and Bochet (*1446*) 1938; Liebegott (*1450*) 1940–41; Bigelow (*1444*) 1943; and Stadie, Riggs, and Haugaard (*1451*) 1944. An unsigned article published in the British Medical Journal in 1942 (*1452*) may also be referred to.

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B. EFFECTS OF INCREASED OXYGEN TENSION NOT IN EXCESS OF ONE ATMOSPHERE

1. GENERAL STUDIES

There is a diversity of opinion in the literature as to the harmful effects of breathing oxygen in concentrations greater than that present in normal air, but at normal atmospheric pressure. It is doubtless true that different animal species show differences in tolerance to hyperoxygenated air or to pure oxygen. Also, the presence or absence of untoward effects depends upon the duration of exposure, and in part upon the condition of the animal at the time of exposure. Quinquaud (*1466*) 1884 stated that dogs breathing pure oxygen at 1 atmosphere for 10 to 30 minutes were not harmfully affected. There was some slowing of the pulse and a general sedative action; the respiratory rate was slower and there was a slight reduction in temperature, with a definite decrease in carbon dioxide excretion. Achard, Binet, and Leblanc (*1453*) 1927 exposed guinea pigs and rabbits continuously to 80 percent oxygen and air mixtures at normal atmospheric pressure. The carbon dioxide level was not allowed to rise above 1 percent. The guinea pigs died in 3 to 5 days while the rabbits survived somewhat longer, succumbing in 5 to 6 days. An increase in the red blood cell count was noted, and the authors also reported a rapid rise in the white blood cell count followed by a sudden drop. On post-mortem investigation, there were congestion and edema of the lungs.

Bounhiol (*1458*) 1929 found that guinea pigs died rapidly in an atmosphere containing 80 to 100 percent oxygen at normal barometric pressure. There was an increase in the red blood cell count, a slowing of the heart rate, and on autopsy, congestion in the lungs, liver, spleen, and other viscera. Rabbits were more tolerant to these hyperoxygenated air mixtures than were guinea pigs, and Bounhiol found that the animals were all capable of adapting themselves to concentrations of oxygen up to 40 percent.

As Bean (*1445*) has pointed out in a brief historical introduction to his review on the effects of oxygen and increased pressure, the clinical use of oxygen in the treatment of disease, particularly disturbances of the respiratory system, was made very soon after its discovery. Priestley himself considered it possible that oxygen might find therapeutic applications. It was not long before the possible harmful effects of high oxygen concentrations began to be investigated, and with the increased use of oxygen in therapy and in inhalation anesthesia, the question of the maximum tolerable concentrations in patients and in healthy human beings assumed great practical importance.

Richards and Barach (*1467*) 1932 treated three patients with pulmonary fibrosis and

extreme cardiorespiratory insufficiency by continuous exposure to air mixtures containing 45 to 50 percent oxygen at normal barometric pressure. One patient was maintained in a chamber containing this oxygen-rich air for 7 hours a day for a period of 6 weeks, and then constantly for 7 months. Another patient was kept in the chamber without interruption for 2 months, and was then given oxygen through a nasal catheter for a further period of 2 months. The third patient was maintained in the oxygen chamber for 10 days, then was given oxygen by nasal catheter for 3 weeks continuously, and subsequently for 5 to 6 hours daily for a period of 8 months. The second patient died, but the other two showed remarkable improvement and were able to tolerate ambulatory activity. It is thus quite apparent that oxygen in these concentrations may be breathed for prolonged periods without harm. However, it does appear that the tolerance of a patient with pulmonary fibrosis may not be the same as that of a normal individual.

Returning to animal experiments, it may be mentioned that in 1937, Pflesser (*1464*) found at normal barometric pressure that mice succumbed in 35 to 44 hours to an 86 to 92 percent concentration of oxygen. On breathing 93 to 97 percent oxygen, cats died in 70 to 86 hours while dogs died after 108 hours of this exposure. The cause of death was stated to be inflammatory changes in the lungs leading to cardiac and circulatory failure.

The effects of high oxygen percentages at reduced barometric pressure are of interest particularly in relation to the use of oxygen by aviators at high altitudes. Armstrong (*1455*) 1938 carried out a series of experiments on rabbits breathing pure oxygen at various simulated altitudes. At sea level, animals died in 72 to 94 hours, and at 5,000 ft. equivalent altitude, death occurred after 142 to 170 hours. In all these animals, there was edema and engorgement of the lungs. At 10,000 ft. equivalent altitude, a few animals died on the eighth to tenth day, while at simulated altitudes of 20,000 to 30,000 ft., no ill effects were encountered. At 35,000 to 40,000 ft., there were evidences of anoxemia and at simulated altitudes between 43,000 and 50,000 ft., animals survived only for a brief period, in spite of the fact that they were breathing 100 percent oxygen. Rapid transfer of these animals from the oxygen mixtures to air always resulted in death. These experiments indicate what has also been found in practical experiments with aviators, that inspiration of oxygen even at high percentages is not harmful under the conditions present in aircraft at altitude.

Fine, Hermanson, and Frehling (*1461*) 1938 found no evidence of oxygen poisoning in patients who inhaled 95 percent oxygen for the deflation of distended intestines or relief of symptoms following encephalography. Orzechowski and Holste (*1462*) 1938 reported on limits of endurable oxygen tensions in rats, and Pflesser (*1465*) 1938 again referred to limits of tolerance to hyperoxygenated air in mice, cats, and dogs. On post-mortem examination, the mice showed edema of the lungs, and, in the dogs and cats, there was injection of the vessels of the trachea and pharynx, edema and emphysema of the lungs, and serous effusions in the body cavities. The heart was soft and flat.

For an experimental study of the effects of hyperoxygenated air on healthy human subjects, the reader is referred to a report in 1939 by Becker-Freyseng and Clamann (*1456*). These workers subjected themselves to 90 percent oxygen at atmospheric pressure, controlling the temperature, humidity, and carbon dioxide concentration. No ill effects were observed during the first 24 hours, but after this time, there was an increase in the body temperature and pulse rate, and a decrease in vital capacity. Paresthesias in the fingertips were noted. On the third day, the body temperature and pulse rate were still increased; there was pain in the knees and elbows with nausea and vomiting. The experiment was terminated after 65 hours. The red blood cell count increased in some cases, or remained practically unchanged in others. There was a slight increase in the white blood cell count. No change in the differential count was seen. By the second day, there was a fall in hemoglobin value. Signs of bronchopneumonia were present. No change in the electrocardiagram was seen throughout the experiment. On

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breathing 90 percent oxygen, there were wide fluctuations in the alveolar carbon dioxide tension, whereas it was constant in normal air.

Becker-Freyseng and Clamann's report contains a good review of previous experiments, and, in a later report by the same authors (*1459*) 1939, there is a discussion of the effects of high oxygen concentrations upon cellular metabolism. Binet, Bochet, and Bryskier (*1457*) 1939 found that mice breathing 95 percent oxygen at normal pressure died in 40 to 50 hours; guinea pigs lived for 60 to 65 hours, while birds survived for 4 to 12 days. There was a slow decrease in the respiratory rate, and the red blood cell count increased in both guinea pigs and birds. There was an increase in the glutathione concentration in the blood, which attained a maximum in 2 days and then decreased. The walls of the alveoli of the lungs were thickened, and there was leucocytic infiltration of the liver and general congestion of the viscera. Breathing 70 percent oxygen, experimental animals survived for 10 to 18 days. After about 6 to 8 hours, the respiratory rate fell to approximately half the normal figure and then remained constant.

Breathing 60 percent oxygen, the animals were apathetic, and respiratory rate was still reduced. However, all animals lived for more than 30 days. Very little change in the red blood cell count was observed. In experimental studies carried out in 1941 by Paine, Keys, and Lynn (*1463*), dogs breathing 99 to 100 percent oxygen at normal atmospheric pressure exhibited respiratory distress after 48 hours, and died in 60 hours. Breathing 90 percent oxygen, animals survived twice as long, while with 80 percent oxygen, no deaths occurred. Autopsies showed congestion and edema of the lungs, pleural effusion, right heart failure, congestion of the liver, contraction of the spleen, and distention of the stomach.

1453. Achard, C., L. Binet, and A. Leblanc. Sur la mort en atmosphère suroxygénée. *C. R. Acad. Sci., Paris*, 1927, *184:* 771–773.

1454. Achard, C., L. Binet, and A. Leblanc. Recherches sur les effets biologiques des milieux suroxygénés. *J. Physiol. Path. gén.*, 1927, *25:* 489–494.

1455. Armstrong, H. G. The toxicity of oxygen at decreased barometric pressures. *Milit. Surg.*, 1938, *83:* 148–151. [P]

1456. Becker-Freyseng, H. and H. G. Clamann, Zur Frage der Sauerstoffvergiftung. *Klin. Wschr.*, 1939 *18:* 1382–1385. [P, R]

1457. Binet, L., M. Bochet, and A. Bryskier. Les atmosphères suroxygénées. *J. Physiol. Path. gén.*, 1939, *37:* 524–535. [P]

1458. Bounhiol, J.-P. Modification du régime de fixation de l'oxygène respiratoire chez les animaux vivant en milieux suroxygénés. *C. R. Soc. Biol. Paris*, 1929, *101:* 684–686. [P]

1459. Clamann, H. G. and H. Becker-Freyseng. Einwirkung des Sauerstoffs auf den Organismus bei höherem als normalem Partialdruck unter besonderer Berücksichtigung des Menschen. *Luftfahrtmed.*, 1939, *4:* 1–10. [P, M, R]

1460. Comroe, J. H., R. D. Dripps, P. R. Dumke, and M. Deming. Oxygen toxicity: The effect of inhalation of high concentrations of oxygen for twenty-four hours on normal men at sea level and at a simulated altitude of 18,000 feet. *J. Amer. med. Ass.*, 1945, *128:* 710–717. [P, M]

1461. Fine, J., L. Hermanson, and S. Frehling. Further clinical experiences with ninety-five percent oxygen for the absorption of air from the body tissues. *Ann. Surg.*, 1938, *107:* 1–13. [P]

1462. Orzechowski, G. and K. Holste. Sauerstoffvergiftung. *Arch. exp. Path. Pharmak.*, 1938, *190:* 198. [P]

1463. Paine, J. R., A. Keys, and D. Lynn. Manifestations of oxygen poisoning in dogs confined in atmospheres of 80 to 100 per cent oxygen. *Amer. J. Physiol.*, 1941, *133:* P 406–407. [P]

1464. Pflesser, G. Beitrag zur Frage der Schädlichkeit des Sauerstoffs. *Arch. exp. Path. Pharmak.*, 1937, *187:* 472–478. [P]

1465. Pflesser, G. Was hat der Praktiker bei der künstlichen Zufuhr von Sauerstoff zu beachten? *Med. Welt.*, 1938, *12:* 1600–1601. [P, M]

1466. Quinquaud, C.-E. Thérapeutique expérimentale et clinique. Les inhalations d'oxygène dans l'atmosphère normale. *C. R. Soc. Biol. Paris*, 1884, Sér. 8, *1:* 687–694. [C, P]

1467. Richards, D. W., Jr. and A. L. Barach. The effects of oxygen treatment over long periods of time in patients with pulmonary fibrosis. *Amer. Rev. Tuberc.*, 1932, *26:* 253–260. [Ch]

2. EFFECTS ON THE CARDIOVASCULAR SYSTEM

As Bean (*1445*) has stated, a study of the evidence leaves little question but that respiration of oxygen or hyperoxygenated air at normal atmospheric pressure results in a slowing of the heart. Reports concerning blood pressure changes are less clear-cut, but it does appear that the pulse pressure is diminished.

Loewy (*1474*) 1894 reported slowing of the heart in animals breathing oxygen, and either no change or a very slight rise in the blood pressure. Benedict and Higgins (*1499*) 1911 found a very definite fall in the pulse rate of human subjects as a result of breathing 40 to 90 percent oxygen at atmospheric pressure, and a similar observation was made by Dautrebande and Haldane (*1493*) 1921. Parkinson (*1475*) 1912 found in human subjects breathing 90 percent oxygen that the pulse rate was usually slowed by about 5 beats per minute. On resumption of air breathing, the pulse returned to its original level. One subject showed an increase in pulse rate while breathing oxygen. Steinhaus, Jenkins, and Lunn (*1476*) 1931 observed no change in the pulse rate of dogs breathing air or oxygen-rich air mixtures. Anthony and Kümmel (*1468*) 1939 found that in man the pulse rate was decreased by breathing oxygen or hyperoxygenated air.

de Waele and Van de Velde (*1477*) in 1939 found that the respiratory rate was diminished in rabbits breathing oxygen-rich air, and attributed this to an effect on the receptors in the auricles.

In 1940, Cusick, Benson, and Boothby (*1470*) found that breathing pure oxygen for 30 minutes produced a reduction in the caliber of both arteries and veins in the human retina, the change being usually more pronounced in the veins. Quantitative measurements of the cerebral blood flow in macaques reported by Dumke and Schmidt (*1471*) 1942–43 indicated that breathing pure oxygen in nembutalized animals produced distinct constrictor action on cerebral vessels. Keys, Stapp, and Violante (*1472*) 1942–43 found a decrease in the pulse rate in human subjects on breathing oxygen or hyperoxygenated air, and a slight but consistent rise in the diastolic blood pressure with a tendency to an increase in the systolic pressure. The pulse pressure fell somewhat. There was a slight increase in cardiac "effort," but no alteration in the size of the heart as indicated by X-ray. In summarizing the effects of oxygen and oxygen-rich mixtures upon the cardiovascular system, it may be stated that the pulse rate is usually diminished while the blood pressure changes are less consistent. There appears also to be a slight vasoconstrictor action in the brain and in the retina.

1468. Anthony, A. J. and H. Kümmel. Herzfrequenz und Herzstromkurve bei Gesunden nach kurzdauernder Sauerstoffatmung. *Z. ges. exp. Med.*, 1939, *106:* 303–313. [P]

1469. Bernthal, T. G., D. W. Bronk, N. Cordero, and R. Gesell. The regulation of respiration. XVIII. The effects of low and high alveolar oxygen pressure and of sodium cyanide on the carotid and femoral flow of blood as studied with the continuous electrometric method. *Amer. J. Physiol.*, 1927–28, *83:* 435–444. [P]

1470. Cusick, P. L., O. O. Benson, Jr., and W. M. Boothby. Effect of anoxia and of high concentrations of oxygen on the retinal vessels; preliminary report. *Proc. Mayo Clin.*, 1940, *15:* 500–502. [P]

1471. Dumke, P. R. and C. F. Schmidt. Quantitative measurements of cerebral blood flow in the macacque monkey. *Amer. J. Physiol.*, 1942-43, *138:* 421–431. [P]

1472. Keys, A., J. P. Stapp, and A. Violante. Responses in size, output and efficiency of the human heart to acute alteration in the composition of inspired air. *Amer. J. Physiol.*, 1942–43, *138:* 763–771. [P]

1473. Lennox, W. G. and E. L. Gibbs. The blood flow in the brain and the leg of man and the changes induced by alteration of blood gases. *J. clin. Invest.*, 1932, *11:* 1155–1177. [P]

1474. Loewy, A. Über die Respiration und circulation unter verdünnter und verdichter, sauerstoffarmer und sauerstoffreicher Luft. *Pflüg. Arch. ges. Physiol.*, 1894, *58:* 409–415. [P]

1475. Parkinson, J. The effect of inhalation of oxygen on the rate of the pulse in health. *J. Physiol.*, 1912, *44:* 54–58. [P]

1476. Steinhaus, A. H., T. A. Jenkins, and J. J. Lunn. The heart rate of dogs breathing normal and oxygen-rich air. *Amer. J. Physiol.*, 1930, *92:* 436–439. [P]

1477. Waele, H. de and J. Van de Velde. La réaction du réflexe hypertenseur des oreillettes à la respiration en air comprimé et à l'excès d'oxygène. *C. R. Soc. Biol. Paris*, 1939, *132:* 312. [P]

3. EFFECTS ON THE BLOOD

In 1916, Karsner (*1529*) found that prolonged exposures to 80 to 90 percent oxygen at normal atmospheric pressure appeared to produce no material changes in the red blood count. In four out of five of Karsner's animals, there was a constant and appreciable leucocytosis. However, Karsner considered that this might have been an accidental variation such as is frequently seen in rabbits. Other

workers, however, have reported definite changes in the blood picture, notably, a decrease in the red blood count. Barcroft, Hunt, and Dufton (*1480*) 1919–20 found that continuous administration of 50 percent oxygen to human patients resulted in a fall in the red blood cell count if the pre-exposure level was above 5 million cu. mm. If the count was less than 5 million, exposure to high oxygen concentration produced no change. Hitzenberger and Molenaar (*1486*) 1934 found that healthy human subjects who breathed pure oxygen at normal barometric pressure for 20 minutes showed a slight increase in the total circulating blood volume. The red blood cell count and hemoglobin values were unchanged. The investigators found a reduction in the average diameter and volume of the red blood cells, the average diameter decreasing from 7.3μ to 7.1μ. There was also a definite reduction in the serum albumin content and the hematocrit value. The results indicate, according to the investigators, a dilution of the blood with tissue fluid, as well as water loss from the erythrocytes.

A decrease in the diameter of the red cells as a result of breathing oxygen was also observed in mice, guinea pigs, and rabbits by Schmidt-Lange and Podlouchy (*1487*) 1937. Gunther (*1484*) 1928 reported a decrease in red blood cell diameter from an average of 7.14μ to 6.72μ on breathing oxygen. According to Anthony and Bechthold (*1478*) 1939, there was a decrease in the hemoglobin concentration of the blood and in the red blood cell count in human subjects within a few minutes after breathing oxygen. This early decrease in the hemoglobin values and the red blood cell count was attributed to a rise in blood volume resulting from a shift in tissue fluids. Anthony and Biedenkopf (*1479*) 1938 noted a decrease in the erythrocyte count of about 7.8 percent and in the hemoglobin concentration of 3.3 percent in 28 subjects after breathing oxygen at atmospheric pressure. After resumption of ordinary air, hemoglobin value rose above the initial level.

Binet and Bochet (*1446*) 1938 found that breathing hyperoxygenated air caused an initial decrease in the red blood cell count, followed by values as high as 150 percent above the normal level. Binet, Bochet, and Guiraud (*1481*) 1939 found that guinea pigs and a rabbit breathing 70 percent oxygen showed a fall in the red blood cell count in the first hour. After 48 hours, the count returned to normal and remained so for several days, after which there was a slowly developing polycythemia. Animals breathing 60 percent oxygen survived for 25 to 30 days. There was a reduction in the erythrocyte count after 2 hours, persisting for 2 to 3 days. After this time, the count became normal again. With 40 percent oxygen, there was a fall in red blood cell count, followed on the fourth day by a return to normal. A human subject breathing 60 percent oxygen in an oxygen tent showed a fall in red blood cell count from 4,800,000 to 4,000,000 after a stay of 45 minutes.

Regarding the oxygen tension in the blood, Smith (*1488*) 1897–98 reported that high oxygen pressure lowers the blood oxygen content, while Tobiesen (*1489*) 1895 found that the quantity of oxygen taken up by the blood was practically uninfluenced by the inhalation of high percentages of oxygen at atmospheric pressure or at increased barometric pressure. Full and Friedrich (*1483*) 1923 reported that in human subjects breathing oxygen at pressures of 16 to 18 cu. mm. H_2O showed a fall in blood sugar, blood chlorides, hemoglobin, and serum albumin. The blood pressure also fell. In these experiments, the duration of inhalation was 30 to 60 minutes and all values except those for chlorides returned rapidly to pre-oxygenation levels. Breathing oxygen-enriched air diminished the rise in the lactic acid content of blood and urine normally resulting from exercise, according to a report by Hewlett, Barnett, and Lewis (*1485*) 1926–27. Davis (*1482*) 1941 reported that oxygen administration to dogs gave no significant change in blood sugar, blood chlorides, or non-protein nitrogen. There was, however, a diminution in the carbon dioxide combining power of the blood, which lasted for as long as 20 minutes after oxygen administration had ceased. For a further discussion of the changes resulting from inhalations of high

concentrations of oxygen, the reader is referred to Bean's review (*1445*).

1478. Anthony, A. J. and K. Bechthold. Der durchmesser menschlichen Erythrocyten bei Sauerstoffatmung. *Z. ges. exp. Med.*, 1939, *105:* 423–429. [P]

1479. Anthony, A. J. and H. Biedenkopf. Der Einfluss kurzdauernder Sauerstoffatmung auf Hämoglobingehalt und Erythrocytenzahl des menschlichen Blutes. I. *Z. ges. exp. Med.*, 1938, *103:* 451–457. [P]

1480. Barcroft, J., G. H. Hunt, and D. Dufton. The treatment of chronic cases of gas poisoning by continuous oxygen administration in chambers. *Quart. J. Med.*, 1919–20, *13:* 179–200.

1481. Binet, L., M. Bochet, and A. Guiraud. Inhalation d'oxygène et hypoglobulie. *C. R. Soc. biol. Paris*, 1939, *130:* 1249–1251. [P]

1482. Davis, H. A. Physiologic effects of high concentrations of oxygen in experimental secondary shock. *Arch. Surg., Chicago*, 1941, *43:* 1–13.

1483. Full, H. and L. v. Friedrich. Wirkung von Sauerstoffüberdruckatmung auf die Blutzusammensetzung. *Klin. Wschr.*, 1923, *2:* 69–72.

1484. Gunther, H. Formproblem an menschlichen Erythrozyten. *Folia haemat., Lpz.*, 1928, *35:* 383–417.

1485. Hewlett, A. W., G. D. Barnett, and J. K. Lewis. The effect of breathing oxygen-enriched air during exercise upon pulmonary ventilation and upon the lactic acid content of blood and urine. *J. clin. Invest.*, 1926–27, *3:* 317–325.

1486. Hitzenberger, A. and H. Molenaar. Der Einfluss von Sauerstoffatmung auf das Blut normaler Menschen. *Klin. Wschr.*, 1934, *13:* 1599–1600. [P]

1487. Schmidt-Lange, W. and F. H. Podlouchy. Erythrocytometer—Bestimmungen an Tieren unter physiologischen und pathologischen Bedingungen, namentlich nach Blutverlusten und Kampfgasvergiftungen. *Z. ges. exp. Med.*, 1937, *101:* 275–306.

1488. Smith, J. L. The influence of pathological conditions on active absorption of oxygen by the lungs. *J. Physiol.*, 1897–98, *22:* 307–318.

1489. Tobiesen, F. Ueber den specifischen Sauerstoffgehalt des Blutes. *Skand. Arch. Physiol.*, 1895, *6:* 273–298.

4. EFFECTS ON RESPIRATION

Regnault and Reiset (*1511*) 1849 found no alteration in the respiration of animals as a result of breathing air containing two or three times the normal concentration of oxygen. In 1859, Birch (*1502*) stated that breathing oxygen had no effect upon the respiration of normal human subjects. In 1896–97, von Terray (*1514*) reported no change in breathing in experimental animals subjected to oxygen concentrations up to 87 percent. According to Hough (*1508*) 1910, the respiratory rate and volume of normal human individuals was decreased by breathing 60 to 80 percent oxygen. In experiments in 1911 by Benedict and Higgins (*1499*) human subjects breathing oxygen experienced no change in the character, depth, or frequency of respiration as compared with breathing normal air. Dautrebande and Haldane (*1493*) 1921 found that breathing oxygen caused an increase in respiration, a slowing of the pulse, a reduction of the rate of blood flow, and a drop in alveolar carbon dioxide pressure.

Greene (*1494*) 1925 stated that in pulmonary inflammation and edema, the rate of oxygen absorption by the lungs is retarded. Carbon dioxide, however, diffuses more rapidly than oxygen, and is therefore easily eliminated. An increase of oxygen in the inspired air results in a maximum increase in hemoglobin saturation of the blood of about 4 percent together with an increase of the amount of oxygen in physical solution in the plasma. This means that in a normal individual, increase in the oxygen concentration in the air above normal levels has little effect in improving oxygen supply to the tissues. Moreover, increasing the oxygen concentration of the air above a certain level results in pulmonary inflammation. On the other hand, decreasing the oxygen content of the air below normal reduces the oxygen tension in the blood.

Barach (*1490*) 1926 found that breathing 60 percent oxygen was without adverse effect on normal rabbits, whereas inhalation of 80 to 85 percent oxygen for 4 to 16 days resulted in fatal pneumonia. Hamburger, Katz, Cohn, and Rubinfeld (*1495*) 1932 reported that in normal human subjects breathing hyperoxygenated air, there was a decrease in both ventilation and vital capacity. Richards and Barach (*1512*) 1934 found a slight increase in pulmonary ventilation in human beings breathing 40 to 50 percent oxygen. Marshall and Rosenfeld (*1497*) 1936 reported that in human subjects breathing pure oxygen, the rate or minute volume of respiration was not affected, but Binet and Bochet (*1491*) 1938 found a decrease in respiratory rate in sub-

jects breathing pure oxygen at atmospheric pressure.

Heck (*1496*) 1941–42, in an experimental study on human subjects, found that breathing of pure oxygen leads to a rise in the minute volume of respiration. The alveolar carbon dioxide tension fell to a level about 6.13 mm. Hg lower than normal after the first half hour to 1½ hours. This was ascribed to a disturbance of the physico-chemical system of the blood arising from a reduction of the arteriovenous oxygen saturation difference, as well as a reduction of the minute volume output of the heart. In unanesthetized dogs, breathing pure oxygen for 6 minutes resulted in a transient diminution in the respiratory minute volume of 11 to 31 percent according to experiments reported in 1942–43 by Watt, Dumke, and Comroe (*1498*). After denervation of the carotid and aortic bodies, no such effect was observed.

In summary of the effect of oxygen and hyperoxygenated air on respiration, there is apparent lack of unanimity in various reports. Bean emphasizes that the more reliable evidence indicates that oxygen administration does cause changes in breathing which are not large, and may be masked by the techniques used in their measurement. The data appear to indicate that in animals, the respiratory minute volume is reduced by inhalation of oxygen. Whether this applies to humans, is not certain.

1490. Barach, A. L. The effects of atmospheres rich in oxygen on normal rabbits and on rabbits with pulmonary tuberculosis. *Amer. Rev. Tuberc.*, 1926, *13:* 293–316.

1491. Binet, L. and M. Bochet. Les atmosphères suroxygénées. *Médicine*, 1938, *19:* 686–694. [P]

1492. Comroe, J. H., Jr., R. D. Dripps, P. R. Dumke, and M. Deming. Effects produced in man by inhalation of high concentration of oxygen for 24 hours. *Amer. J. med. Sci.*, 1945, *209:* 814.

1493. Dautrebande, L. and J. S. Haldane. The effects of respiration of oxygen on breathing and circulation. *J. Physiol.*, 1921, *55:* 296–299.

1494. Greene, C. W. Oxygen want in health and disease. *J. Amer. med. Ass.*, 1925, *85:* 645–650.

1495. Hamburger, W. W., L. N. Katz, D. J. Cohn, and S. H. Rubinfeld. Observations on the effects of oxygen therapy. I. Clinical observations in heart disease. *J. Amer. med. Ass.*, 1932, *98:* 1779–1783.

1496. Heck, E. Wirkung hoher Sauerstoffteilddrucke auf die Atmung. I. *Luftfahrtmed.*, 1941–42, *6:* 105–113. [P, M]

1497. Marshall, E. K., Jr. and M. Rosenfeld. Depression of respiration by oxygen. *J. Pharmacol.*, 1936, *57:* 437–457. [P]

1498. Watt, J. G., P. R. Dumke, and J. H. Comroe, Jr. Effects of inhalation of 100 per cent and 14 per cent oxygen upon respiration of unanesthetized dogs before and after chemoreceptor denervation. *Amer. J. Physiol.*, 1942–43, *138:* 610–617. [P]

5. EFFECTS ON METABOLISM

As Bean (*1445*) has noted, Seguin and Lavoisier in 1789 performed experiments from which they concluded that respiration of pure oxygen did not produce any alteration of the vital metabolic processes, and that respiration and circulation were neither accelerated nor retarded. In a significant report published in 1849, Regnault and Reiset (*1511*) found no change in the oxygen consumption or the respiratory quotient in animals breathing high concentrations of oxygen. No difficulty was experienced by a hen breathing 65.83 percent to 58.08 percent oxygen for 90 hours. Actually the hen even laid two eggs during the time spent in the chamber. A rabbit remained for 76½ hours in the chamber, breathing oxygen concentrations varying from 54.78 to 31.16 percent without any abnormal symptoms. A rabbit remained for 23 hours and 40 minutes in an oxygen concentration of 72.38 percent without harm, and a dog survived a period of 21 hours in the chamber in oxygen concentrations of 46.63 to 45.17 percent with no apparent adverse effect. Experiments were also carried out in which hydrogen replaced nitrogen in the gas mixtures. In these gases, there was some increase in oxygen consumption.

Birch (*1502*) in 1859 reported that the temperature of normal animals usually rose first and then fell, while breathing oxygen at normal pressure. He considered that oxygen inhalation might raise the temperature in certain disease conditions, but considered that in healthy individuals the temperature was altered only in rare instances.

Paul Bert (*16*) 1878 found that animals breathing oxygen mixtures equivalent to a 48.7 percent concentration showed a rise in oxygen consumption greater than when

breathing either higher or lower oxygen concentrations. He concluded that there was an optimum percentage of oxygen for metabolic activity. Lukjanow (*1509*) 1883–84 carried out experiments with rats, guinea pigs, dogs, cats, doves, and canaries. In none of these experiments was a relation found between oxygen partial pressure in the inspired air and oxygen absorption. A similar finding was reported in 1884 by Frédéricq (*1506*) who found no increase in the oxygen consumption when oxygen-rich mixtures were breathed, in experiments carried on himself and on rabbits. However, the oxygen consumption was diminished on respiration of oxygen-poor mixtures. From experiments carried out principally on dogs, Quinquaud (*1510*) 1884 concluded that it was possible to hyperoxygenate the blood by breathing pure oxygen. By this means, he believed that an additional 2.2 volumes percent of oxygen could be carried in the arterial blood. As a result of such oxygen breathing, there was a fall in rectal temperature, a slight diminution in carbon dioxide exhalation, and a reduction of metabolism. de Saint-Martin (*1513*) in 1884 concluded, on data considered questionable by Bean (*1445*), that chemical phenomena of respiration are not appreciably changed by breathing oxygen-enriched air, and von Terray (*1514*) 1896–97 also concluded that breathing oxygen-rich air did not significantly alter the total metabolism of experimental animals. With oxygen percentages of 10.5 to 87 percent, the metabolic rate was independent of the oxygen content of the inspired air. At the same time, von Terray (*1514*) found that output of carbon dioxide was somewhat diminished. Hill and Macleod (*1507*) 1902 also found a definite decrease in the carbon dioxide excretion on breathing pure oxygen. There was a diminution in the oxygen absorption. From their experiments, they concluded that breathing pure oxygen did cause a distinct decrease in metabolic activity.

Durig (*1504*) in 1903 concluded from experiments on animals and man that oxygen consumption was not increased by breathing oxygen-rich air, and Winterstein (*1515*) 1906 could find no evidence of oxygen storage in the isolated spinal cord of frogs, even when exposed to excess oxygen. Hough (*1508*) 1910 reported that when subjects breathed into a closed container filled with a 60 to 80 percent oxygen mixture, the minute volume and the rate of respiration showed a distinct reduction over control experiments in which normal air was breathed. This reduction began in the first minute. After about 8 minutes, the rate suddenly increased. Hough questioned the soundness of the usual view that the consumption of oxygen by the cell is independent of the amount of oxygen provided by the blood. However, Benedict and Higgins (*1499*) 1911 found no change in the metabolism of human subjects completely at rest breathing air or 40, 60, or 90 percent oxygen. Moreover, there was no change in the type, depth, and rate of respiration. The pulse rate decreased somewhat with increasing oxygen percentage. In three out of six subjects, the oxygen consumption was found to be greater with the 40 percent oxygen mixtures than with higher (60 to 90 percent) or lower (20 percent) oxygen mixtures. In one subject, the oxygen consumption with the 40 percent oxygen mixture was 3 percent above that of the same subject with the 20 percent mixture. Benedict and Higgins (*1499*) considered that these differences in oxygen consumption were insignificant and did not believe that their findings confirmed Paul Bert's view that oxygen consumption was increased by inspiration of a critical oxygen concentration. Hill (*1083*) 1912 also criticized the validity of Bert's assumption.

It may be noted, on the other hand, that Clark-Kennedy and Owen (*1503*) 1926–27 did report an increase in the oxygen uptake on breathing 26 percent oxygen. These investigators also reported a diminution in the respiratory quotient, and an increase in carbon dioxide exhalation. On breathing a 16 percent oxygen mixture, the findings were reversed. Richards and Barach (*1512*) in 1934 subjected healthy, normal men to a 45 percent oxygen mixture in an oxygen chamber for 1 week. At the end of this time, there was a slight decrease in the oxygen capacity of the blood, attributed to the fact that the subjects remained in bed. There was, however, no change in the metabolic rate as measured by

the carbon dioxide output. The pulse rate showed a decrease.

Binet and Bochet (*1501*) in 1937 reported that in a perfused lung preparation, the amount of reduced glutathione diminishes on ventilation with pure oxygen and rises on respiration with nitrogen. In chloralosed dogs, respiration of low oxygen mixtures, equivalent to 8,000, 9,000, 10,000 and 12,000 m. altitude for 2 or 3 hours resulted in a reduction in the total glutathione content of the blood and no change in the percentage of glutathione in the liver. In the spleen and muscles, a reduction of 20 to 27 percent was found. The investigators found that rabbits breathing 96 to 98 percent oxygen at normal barometric pressure survived for an average of approximately 70 hours. Animals sacrificed after 4 hours, 24 hours, 2 days, or 3 days exhibited a notable increase in the percentage of total glutathione in the blood, lungs, kidneys, and liver.

In summarizing the effects of oxygen and hyperoxygenated air at normal barometric pressure upon the metabolic processes, Bean (*1445*) concluded that there was no consistent and dependable evidence to be derived from the literature that breathing oxygen-rich air or pure oxygen causes any alteration in metabolism as manifested by exchange of respiratory gases. Most reports support the view that the respiratory exchange is not a function of oxygen tension, except under conditions when the oxygen tension falls below normal. Bernthal (*1500*) 1938 stated, for example, that very small decreases in the oxygen content of the atmosphere below normal cause distinct alterations in respiratory and circulatory mechanisms, and von Euler, Lijestrand, and Zotterman (*1505*) 1939 concluded that such alterations in respiratory and circulatory activity indicate that low oxygen does produce fundamental alterations in metabolism.

1499. Benedict, F. G. and H. L. Higgins. Effects on men at rest of breathing oxygen-rich gas mixtures. *Amer. J. Physiol.*, 1911, *28:* 1–28. [P]

1500. Bernthal, T. Chemo-reflex control of vascular reactions through the carotid body. *Amer. J. Physiol.*, 1938, *121:* 1–20.

1501. Binet, L. and M. Bochet. Anoxie, hyperoxie et glutathion tissulaire. *C. R. Soc. Biol. Paris*, 1937, *126:* 674–676. [P]

1502. Birch, S. B. On oxygen as a therapeutic agent. *Brit. med. J.*, 1859, N. Ser., pp. 1033–1035; 1053–1055.

1503. Clark-Kennedy, A. E. and T. Owen. The effect of high and low oxygen pressure on the respiratory exchange during exercise. *J. Physiol.*, 1926–27, *62:* xiv–xviP. [P]

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6. EFFECTS ON THE CENTRAL NERVOUS SYSTEM

While the effects of oxygen and oxygen-rich air mixtures at normal barometric pressure are predominant upon the respiratory, circulatory, and metabolic processes, nevertheless, exposure to oxygen or hyperoxygenated air at normal barometric pressure does affect, to some extent, the functions of the central nervous system. Moody and Howard (*1520*) in 1942 reported convulsions in a 2-year-old child suffering from lobar pneumonia who had remained in an oxygen tent during most of the time for approximately a week. Since the convulsive seizures ceased when the patient was removed from the oxygen atmosphere, it seemed reasonable to suppose that the central nervous manifestations were due to oxygen. Obviously, however, many other factors may have been in operation to have caused the convulsions, and it must be admitted that at atmospheric pressure, even pure oxygen does not ordinarily cause convulsive seizures.

Davidson (*1519*) 1925–26 reported that in human subjects breathing pure oxygen at normal pressures, there was at first a slight fall in the reaction time, occurring in the first 10 minutes. This was followed by a return to normal. Barach (*1517*) 1941 has stated that in patients with emphysema and pulmonary fibrosis, respiration of 50 percent oxygen may produce depressant effects upon mental activity, and there mav be sleepiness, stupor, and even coma.

Of particular interest in connection with central nervous system effects of oxygen at normal barometric pressure is the so-called "paradoxical oxygen effect" observed on administration of oxygen under conditions of anoxia. For example, Schwarz and Malikiosis (*1521*) 1938 reported that when subjects were taken in a decompression chamber to an equivalent altitude of 6,500 m. and then given oxygen to breathe, there was a slowing of the pulse within about 15 seconds, as well as a fall in systolic and diastolic blood pressure, followed by a rise. Of particular note were various motor, sensory, and mental disturbances, including tremors, clonic movements of the hands, faulty decisions, disturbed intellectual capacity, and sometimes complete collapse. In some cases, there was uncertainty, anxiety, and a feeling of faintness, as in hyperventilation. The subjects showed poor performance on the handwriting test, there being irregularity in performance, more frequent mistakes, and perseveration. The oxygen saturation of the arterial blood was increased. In discussing the mechanism of this effect of oxygen, the authors consider that high oxygen tensions appear to act as a direct cellular poison on the central nervous system.

Campbell and Hoff (*1517a*) and several others have observed acute convulsive episodes in animals suddenly returned to normal barometric pressure after exposure to simulated high altitudes without supplementary oxygen. In Campbell and Hoff's experiments, young mature monkeys (Macaca mulatta) were subjected to simulated high altitudes by decompression without added oxygen to barometric pressures between 250 and 180 mm. Hg for 44 to 95 minutes. During the decompression, muscular tremors and convulsive manifestations involving the face, limbs, and trunk were observed at the low pressure levels. In all cases, decompression was carried out to the point of apnea and then recompression effected within a few seconds. On return to normal air, the animals gasped and within a minute or so, approximately normal respiration was reestablished. In many cases the animals suffered violent twitching of the muscles of the face or the limbs, progressing in some instances, to generalized convulsions which persisted for several minutes. The mechanism underlying these recompression convulsions is not clear.

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1520. Moody, E. and W. M. Howard. Probable oxygen poisoning produced in an ordinary oxygen tent. Report of case. *Arch. Pediat.* 1942, *59:* 458–460.

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7. PATHOLOGICAL CHANGES

Prolonged exposure to oxygen concentrations of approximately 60 percent or less at atmospheric pressures may apparently be tolerated by animals or human subjects without adverse pathological effects. An observation by Moir (*1534*) in 1895–96 is applicable in this connection. He found that mules kept continuously in the Hudson tunnel operations at about 30 lb. pressure corresponding to approximately 60 percent oxygen for many months remained in perfectly good health and showed no adverse effects. This has been taken to mean that oxygen in concentrations equivalent to 60 percent of 1 atmosphere is innocuous. However, this conclusion does not necessarily follow since a high oxygen percentage at normal barometric pressure is not precisely equivalent in its possible effects upon the organism to normal air breathed at a raised barometric pressure, even though the oxygen tensions in the two cases are the same.

Smith (*1537*) 1899 investigated the pathological effects of increased oxygen tension in the respired air upon mice, birds, guinea pigs, and rats. Exposure of mice to an oxygen tension equivalent to 41.6 percent of 1 atmosphere had no effect after 8 days. In an experiment in which the oxygen tension was raised to a level equivalent to 73.6 percent of 1 atmosphere, one mouse died on the fourth day and one survived for 8 days. At an oxygen pressure of 1.3 atmospheres, mice were at first stimulated by the high oxygen tension. Within 48 hours they became sluggish, dying in 90 hours. The lungs were found to be congested and the spleen enlarged. At an oxygen pressure of 1.8 atmospheres, birds and mice died of pneumonia in about 24 hours. At an oxygen pressure of 2.3 atmospheres, mice began to manifest respiratory difficulties in 10 hours, but recovered when removed to normal air. At an oxygen pressure of 3.6 atmospheres, mice were dead in 5 hours. The alveoli of mice, birds, rats, guinea pigs, and pigeons exposed to oxygen at 1 atmosphere were congested and filled with exudate. There was also congestion of other organs, especially the liver, spleen, and kidneys.

Brüning (*1525*) 1912 reported that exposure of mice to oxygen or compressed air (1.1 atmospheres) for 6 to 24 hours led to hyperemia of the lungs. Brüning stated that no lung damage occurred as a result of breathing oxygen after air or oxygen was humidified to 60 to 80 percent. David (*1527*) in 1912 stated that in animals exposed to pure oxygen at normal barometric pressures, there were changes in the lungs characterized by hyperemia, edema, atelectasis, and inflammation. Karsner (*1529*) in 1916 studied the effect on rabbits of breathing 80 to 90 percent oxygen at normal barometric pressure. In these animals there was a tendency toward dilatation of the heart, particularly of the right side. In many cases, there were cloudy swelling and coarse granulation in the protoplasm and nonsuppurative interstitial myocarditis. No pathological changes were seen in the aorta or in the other blood vessels. In the lungs of animals exposed for 48 hours, there were edema and fibrin deposits, as well as swelling and desquamation of the alveolar epithelium. After 3 days the lungs were edematous and inflamed and showed evidences of pneumonia, probably of irritative origin, described as a fibrinous broncho-pneumonia. The liver was passively congested and there were submucous hemorrhages in the stomach wall. Congestion was also apparent in the kidneys and spleen. No specific changes were seen in the bone marrow, the adrenals, or the blood, but in some animals albuminuria was present. A wide individual variation was found in susceptibility to the poisonous effects of oxygen.

In a further study of the pathological effects of atmospheres rich in oxygen, Karsner and Ash (*1530*) 1916–17 reported no ill effects in

rabbits on breathing 53 percent oxygen for 3 days and 16½ hours. Animals which were kept in an atmosphere of 67 percent oxygen for 3 days and 18½ hours showed no symptoms, but moderate congestion of the lungs was observed upon sacrifice and autopsy. Breathing 60 to 70 percent oxygen for 11 days resulted in no clinical ill effects in rabbits. One animal showed no adverse influence on autopsy while in two others the lungs were congested and edematous, and there was slight desquamation of the alveoli. A rabbit breathing 75 percent oxygen died after 10 days' exposure, showing marked congestion of the abdominal viscera and consolidation of the lungs. Other animals remained alive, but were weak and dyspneic after 11 days' exposure to 75 percent oxygen and showed generalized congestion of the abdominal viscera.

Binger, Faulkner, and Moore (*1522*) 1927 exposed dogs, rabbits, guinea pigs, and mice to 80 percent oxygen at normal barometric pressure. The animals became drowsy and lost their appetites, and gradually became dyspneic and cyanotic. Death was attributed to acute oxygen want arising from destructive lesions of the lungs. Faulkner and Binger (*1528*) 1927 found that frogs were noticeably unaffected by oxygen tension up to 95 percent at normal barometric pressures, and it was found that turtles also were able to tolerate 95 percent oxygen. However, if the oxygen was warmed to 37.5° C. then the response of these poikilothermous animals was the same as that of mammals. Boycott and Oakley (*1523*) 1932 found that on breathing 95 to 99 percent oxygen at normal barometric pressure, one-half of the experimental animals (rats) died. The lungs were collapsed and the tissues of the mediastinum and chest wall were soggy, and there was an effusion of fluid into the pleural cavities. Death was ascribed to this massive pleural effusion. The clinical course in these animals was characteristic; on the fourth day they all developed dyspnea, became cyanotic, and some died 2 days later. Some animals recovered. Dyspneic rats returned to normal air died within about a half-hour.

Smith, Bennett, Heim, Thomson, and Drinker (*1536*) 1932 exposed rats to an air pressure of 3,040 mm. Hg (4 atmospheres, absolute). Rats varying in age from 9 to 40 days showed no disturbance as a result of this experiment. One-hundred-day-old rats after 4 days of exposure showed hypertrophy of the alveolar cells and other pathological features in the lung, such as perivascular edema and cellular infiltration. Animals of 5 months of age showed marked pathological changes in the lungs after 4 days of exposure. The lungs were mottled with beefy red and purple patches, and there were edema and pleural effusion of pale yellow serous fluid. The alveoli were found to be filled with granular, serous exudate which contained fibrin and red blood cells. There was marked emphysema and the alveolar capillaries were engorged with blood. Rats surviving beyond the fourth day showed hyperplasia and hypertrophy of the alveolar cells.

Clamann, Becker-Freyseng, and Liebegott (*1526*) 1940–41 exposed white mice, rats, guinea pigs, rabbits, goats, and dogs to an atmosphere containing 80 to 90 percent oxygen at normal barometric pressure for 1 week. With the exception of the mice and rats, there was at first drowsiness and loss of appetite; then followed dyspnea, leading in some cases to death. One of the guinea pigs died, but only a few mice, rats, and dogs were so affected. In the animals that succumbed, there was a pathological picture of broncho-pneumonia, with serous exudation and necrosis of the alveolar membranes. The authors considered that the pathological changes in the lungs led to diminished oxygen uptake, in spite of an excess oxygen concentration in the inspired air. Further observations on the effects of the prolonged administration of high oxygen concentrations were carried out by Paine, Lynn, and Keys (*1535*) 1941–42. Dogs breathing hyperoxygenated air containing over 75 percent oxygen became lethargic, dyspneic, and refused to eat. When exposed to atmospheres containing 95 to 100 percent oxygen at normal barometric pressure, dogs died in about 39 hours. The lungs, liver, and kidneys were congested and hyperemic. There was a marked atrophy of the hepatic parenchyma in the central part of the lobules. Definite pathological

lesions were found in a number of exposed animals which had shown no symptoms or clinical signs of the damaging action of oxygen.

In 1942, Kaunitz (*1531*) observed myocardial damage in mice as a result of high oxygen tension. The experimental animals were exposed in an oxygen chamber to pure oxygen at 1 atmosphere for 2 to 3 days. On the second day, the animals became apathetic and were unable to eat, and on the third day thev became dyspneic and died. Post-mortem inspection showed evidences of bronchial obstruction, pulmonary atelectasis, and edema, as well as generalized visceral congestion. There were degeneration and fragmentation of cardiac muscle fibers and capillary dilatation within the myocardium. Kaunitz claimed that while at first the oxygen reaches the alveoli with ease, later the bronchi become filled with mucous, and so obstruct the air passages that the resulting decrease in intra-alveolar pressure causes the alveoli to collapse. The myocardial lesions were explained as secondary to the anoxemia arising from the lung damage. In a later report published in 1945, Kaunitz (*1532*) reviewed previous work on the physiological effects of oxygen-rich air. He pointed out that some mice exposed to pure oxygen showed convulsive manifestations and all were cyanotic. The lungs were collapsed and dark red in color, and resembled liver in consistency. The heart, liver, and kidneys were reported to be swollen, the trachea edematous, and the tracheal mucosa denuded of epithelium. There were also edema of the walls of the bronchi and atelectasis of the lungs. The alveolar walls were thickened and the alveolar spaces filled with a transudate containing fibrin and red blood cells. The lung capillaries were enormously engorged. There was no polymorphonuclear leucocytic reaction. Morphologically, the pathological reaction resembled the irritative reaction seen with certain types of war gases. Death was ascribed to profound anoxemia consequent to damage to the alveolar membranes of the lungs, diminished vital capacity, and reduced cardiac output.

Maréchaux (*1533*) in 1943 reported investigations of the pathological effects of breathing 81.5 percent oxygen at normal barometric pressure on cats, dogs, or rabbits which had been unilaterally or bilaterally vagotomised. All animals showed broncho-pneumonic inflammation with exudation, edema, emphysema, and swelling of the vascular walls.

For a more detailed survey and analysis of the pathological changes occurring as a result of exposure to oxygen or hyperoxygenated air at normal barometric pressure, the reader should consult Bean's review. He summarizes the outstanding pathological changes as follows:

(*a*) Inflammation, congestion, edema, atelectasis, fibrin formation, and consolidation of the lungs.

(*b*) Pneumonia of various types.

(*c*) Bronchitis with bronchiectasis.

(*d*) Hypertrophy, hyperplasia, desquamation, and degenerative changes in alveolar cells.

(*e*) Sclerotic changes with narrowing, thickening, and hyalinization of the pulmonary arterioles.

(*f*) Dilatation of the right or both sides of the heart.

(*g*) Hypertrophy and cloudy swelling of the myocardium.

(*h*) Congestion of the abdominal viscera and cloudy swelling of the kidneys.

(*i*) Splenic contraction.

(*j*) Testicular degeneration.

Bean concludes that there is little question but that continuous exposure of laboratory animals to oxygen in concentrations greater than 60 to 70 percent at normal barometric pressure for 12 to 14 hours or even less produces pathological changes especially in the lungs, and that if exposure is prolonged further, these changes often prove fatal. Although the onset of the deleterious effect on human subjects may be longer delayed than in other animals, Bean states that there is good reason to believe that man is similarly affected.

1522. Binger, C. A. L., J. M. Faulkner, and R. L. Moore. Oxygen poisoning in mammals. J. exp. Med., 1927, *45:* 849–864, 2 pls. [P]

1523. Boycott, A. E. and C. L. Oakley. Oxygen poisoning in rats. *J. Path. Bact.*, 1932, *35*(1): 468–469. [P]

1524. Brüning, A. Ueber Sauerstoffvergiftung. *Dtsch. med. Wschr.*, 1912, *38:* 1651. [P]

1525. Brüning, A. Studien zur Narkosenfrage, insbesondere über die Anwendung von Sauerstoff und komprimierter Luft. *Dtsch. Z. Chir.*, 1912, *113:* 532–581. [P, B]

1526. Clamann, H. G., H. Becker-Freyseng, and G. Liebegott. Das allgemeine Verhalten und die morphologischen Lungenveränderungen verschiedener Tierarten bei langer Einwirkung erhöhten Sauerstoffteildrucks. *Luftfahrtmed.*, 1940–41, *5:* 17–23. [P]

1527. David, O. Versuche zur Erzeugung von Lungenhyperämie. *Z. klin. Med.*, 1912, *74:* 404–427. [P]

1528. Faulkner, J. M. and C. A. L. Binger. Oxygen poisoning in cold blooded animals. *J. exp. Med.*, 1927, *45:* 865–872. [P]

1529. Karsner, H. T. The pathological effects of atmospheres rich in oxygen. *J. exp. Med.*, 1916, *23:* 149–170, 4 pls. [P]

1530. Karsner, H. T. and J. E. Ash. A further study of the pathological effects of atmospheres rich in oxygen. *J. Lab. clin. Med.*, 1916–17, *2:* 254–255. [P]

1531. Kaunitz, J. Myocardial damage resulting from high oxygen tension. *J. Aviat. Med.*, 1942, *13:* 267-271. [P]

1532. Kaunitz, J. The effect of high oxygen tension on the respiratory system. *J. Mt. Sinai Hosp., N. Y.*, 1945, *12:* 411–415. [M, R]

1533. Maréchaux, E. W. Über die Wirkung von Sauerstoff erhöhten Teildruckes auf lungengeschädigte Tiere. *Arch. exp. Path. Pharmak.*, 1943, *201:* 213–233. [P]

1534. Moir, E. W. Tunnelling by compressed air. *J. R. Soc. Arts*, 1895–96 *44:* 567–585.

1535. Paine, J. R., D. Lynn, and A. Keys. Observations on the effects of the prolonged administration of high oxygen concentration to dogs. *J. thorac. Surg.*, 1941–42, *11:* 151–168. [P]

1536. Smith, F. J. C., G. A. Bennett, J. W. Heim, R. M. Thomson, and C. K. Drinker. Morphological changes in the lungs of rats living under compressed air conditions. *J. exp. Med.*, 1932, *56:* 79–89, pls. 2–5. [P]

1537. Smith, J. L. The pathological effects due to increase of oxygen tension in the air breathed. *J. Physiol.*, 1899, *24:* 19–35. [P]

8. TOLERANCE AND ACCLIMATIZATION

Different species vary in their tolerance to oxygen and their susceptibility to its poisonous effects. For example, Schloesing and Richard (*1544*) stated in 1896 that the swim bladders of deep sea fish contain oxygen in concentrations as high as 84.6 percent. At depths of 4,500 ft. where these creatures live, the oxygen pressure would be equivalent to 115 atmospheres of pure oxygen. Clearly, therefore, some tissues are immune to very high tensions of oxygen. A number of observations have been made by Campbell upon acclimatization to oxygen, and for a more detailed comment on these studies, the reader is referred to Bean's review (*1445*). Campbell (*1540*) 1927 found that cats, unlike most animals, were unable to tolerate prolonged exposure to oxygen at a pressure corresponding to 60 percent of 1 atmosphere. Animals lost appetite and became weak, and the lungs showed evidence of collapse and congestion. High oxygen concentrations at normal barometric pressure lead to a fall in hemoglobin value and red blood cell count in monkeys, rabbits, rats, guinea pigs, and mice. There was an inverse relationship between the hemoglobin percentage and the oxygen pressure in the inspired air. However, the changes in hemoglobin are not essential to acclimatization.

Evans (*1541*) in 1927 was doubtful of the validity of comparisons of oxygen tolerance of animals with that of humans suffering from pulmonary diseases. He questioned whether the normal individual is harmed by breathing oxygen concentrations as high as 80 to 100 percent for 1 or several days. That changes in the lungs caused by earlier disease processes may affect the tolerance of the organism to oxygen or hyperoxygenated air is suggested by the findings of Nelson and Gowan (*1543*) 1930 that in young rats less than 3 to 4 months old, pneumonia was relatively infrequent. It seems possible that the greater resistance of rats under 3 months of age to oxygen poisoning may be due to the absence of preexposure pathology in the younger animals. Smith, Heim, Thomson, and Drinker (*1545*) 1932 found that white rats exposed at optimum conditions of temperature and humidity to an air pressure of 4 atmospheres (absolute) developed acute oxygen poisoning on the third or fourth day. The surviving rats recovered, although the weight remained lower than in the controls. After 72 days of exposure, the surviving animals were decompressed to normal atmospheric pressure. Twenty-eight percent of the animals died on decompression or on the following day. The survivors were kept

in normal air for 40 days and then recompressed. There were no signs of oxygen poisoning on the second compression. Rats under 3 months of age, as has been said, showed no signs of oxygen poisoning. Of the litter born to females during the first exposure, none survived. On exposure of the rat early in pregnancy, it was found that the litter had a reasonable chance of survival. All rats dying during exposure to high oxygen pressure or decompression to normal atmospheric pressure showed evidences of hyperemia and edema of the lungs. Death was ascribed to broncho-pneumonia. Rats far advanced in pregnancy were considered to be more susceptible to oxygen poisoning in compressed air than nonpregnant animals. This was ascribed to respiratory embarrassment due to the encroachment by the gravid uterus upon the thoracic cavity.

Soulié (*1546*) 1939 discussed experimental modifications of individual resistance of certain animals to the toxic action of oxygen, and Barach, Eckman, Oppenheimer, Rumsey, and Soroka (*1539*) 1944 found that the resistance of rats to oxygen poisoning was raised by a gradual increase in oxygen concentration from 60 percent to approximately 100 percent. Increased tolerance could be developed also by direct exposure to pure oxygen with four daily periods of return to atmospheric air totalling 60 minutes a day. By gradually increasing the oxygen concentration, the death rate of rats for the first 4 days in 100 percent oxygen fell from 96 percent in control rats to 7 percent in acclimatized animals. By the method of periodic return to normal air, there was a mortality of 33 percent within 8 days, and a survival time of 27 days for the remaining 67 percent. In the unacclimatized control group, 99 percent of the animals died within 8 days. Mice, rabbits, and guinea pigs developed no increase in resistance to pure oxygen by the method of gradually increasing the concentration. The acquired tolerance in rats persisted for 2 months.

Barach (*1538*) 1934 and others took the view that the use of oxygen by patients in concentrations above 60 percent was dangerous. This view has been modified by a number of investigators and it is now generally accepted that oxygen in percentage from 80 to 100 percent may be safely administered at atmospheric pressure for a considerable period of time with proper precautions. Evans (*1541*) 1939, for example, reported that he had inhaled pure oxygen for 4 hours a day for several days without apparent harmful effects; this investigator claimed that the pneumonic lung has a higher tolerance for oxygen than a normal lung.

1538. Barach, A. L. The treatment of asphyxia in clinical disease, with especial reference to recent developments in the use of oxygen in heart disease. *N. Y. St. J. Med.* 1934, *34:* 672–681. [P]

1539. Barach, A. L., M. Eckman, E. T. Oppenheimer, C. Rumsey, Jr., and M. Soroka. Observations on methods of increasing resistance to oxygen poisoning and studies of accompanying physiological effects. *Amer. J. Physiol.* 1944, *142:* 462–475. [P]

1540. Campbell, J. A. Further observations on oxygen acclimitization. *J. Physiol.*, 1927, *63:* 325–342. [P]

1541. Evans, J. H. Oxygen therapy in pneumonia. *Curr. Res. Anesth.*, 1927, *6:* 57–63.

1542. Evans, J. H. A plea in behalf of the anoxemic patient. *N. Y. St.* J. Med., 1939, *39:* 709–717. [P]

1543. Nelson, J. B. and J. W. Gowan. The incidence of middle ear infection and pneumonia in albino rats at different ages. *J. infect. Dis.*, 1930, *46:* 53–63. [P]

1544. Schloesing, T., Jr. and J. Richard. Recherche de l'argon dans les gaz de la vessie natatoire des Poissons et des Physalies. *C. R. Acad. Sci., Paris,* 1896, *122:* 615–619.

1545. Smith, F. J. C., J. W. Heim, R. M. Thomson, and C. K. Drinker. Bodily changes and development of pulmonary resistance in rats living under compressed air conditions. *J. exp. Med.*, 1932, *56:* 63–78. [P]

1546. Soulié, P. Modifications expérimentales de la résistance individuelle de certains animaux à l'acion toxique de l'oxygène. *C. R. Soc. Biol. Paris*, 1939, *130:* 541–542. [P]

C. TOXIC EFFECTS OF OXYGEN TENSIONS IN EXCESS OF ONE ATMOSPHERE

1. GENERAL STUDIES ON THE POISONOUS ACTION OF OXYGEN AT PRESSURES GREATER THAN 1 ATMOSPHERE

For a detailed survey of the toxic effects of oxygen at pressures greater than 1 atmosphere, the reader should consult the review by Bean (*1445*) published in 1945. As he has pointed out, many of the changes induced by

oxygen-enriched air or pure oxygen at normal barometric pressure are also observed under conditions in which the body is exposed to oxygen tensions greater than 1 atmosphere. There are other additional and quite distinct toxic effects which are characteristic of the action of oxygen at higher barometric pressures and these toxic effects result from etiological factors which may not be operating at lower oxygen tensions, and which may be complex. Convulsive manifestations tend to dominate the clinical picture of oxygen poisoning at the higher pressures, while the pulmonary pathological manifestations are the prominent feature of the clinical symptomatology at oxygen tensions of 1 atmosphere or less.

For pioneer work on oxygen poisoning, we are indebted to the genius of Paul Bert who not only confirmed Hoppe's gas bubble theory of the etiology of decompression sickness and greatly extended our knowledge in this field, but also clearly recognized the relation between convulsive attacks and the intensity of the oxygen pressure. The reader is advised to consult Paul Bert's monograph (which is available in an English translation) (*16*) 1878 as a preliminary study to any investigation of the harmful effects of oxygen at elevated barometric pressures. The reader will also find the comments on Bert's work by Bean (*1445*) especially useful.

Phillipon (*1556*) 1893 subjected ducks to compressed oxygen at a pressure of 6 atmospheres. Death occurred in about 20 minutes. If removed from the chamber in a quarter of an hour, the animals, after convulsions, died in several minutes. If animals maintained for one-quarter of an hour at an oxygen pressure of 5 atmospheres were suddenly decompressed, followed by recompression (before death could supervene) to an air pressure of 5 atmospheres and then slowly decompressed (within a period of 5 to 6 minutes), the animals left the chamber without any apparent subsequent ill effects. These experiments were repeated with similar results using mammals.

Bornstein and Stroink (*1549*) 1912, in experiments on one of themselves, found that after breathing oxygen at a pressure of 2 atmospheres above normal while exercising on a bicycle, there were cramps in the hands and legs after 51 minutes. The cramps subsided on decompression, but the patellar reflexes were absent for several hours. Experiments with animals indicated that oxygen at an absolute pressure of 5 atmospheres could be endured for periods up to 6 hours, while an oxygen pressure of 7 atmospheres (absolute) was tolerable for only three-quarters of an hour to 1 hour.

Oxygen poisoning is not limited to the higher organisms. Cleveland (*1550*) 1925 found that parasitic protozoa in termites were killed by exposure of the termites to an oxygen pressure of 3.5 atmospheres in 30 minutes. With this treatment, the termites were uninjured, but after 45 hours, the termites themselves were killed. Cockroaches succumbed under these conditions after 90 hours and frogs survived for 65 hours at an oxygen pressure of 3.5 atmospheres. Rats were unable to survive longer than 6 hours. In some animals, parasitic protozoa were not killed. The possibility of utilizing exposure to high oxygen pressures in defaunating animals without injury is raised by these observations; and further investigations are indicated. Should it be shown that pathogenic protozoa, such as the malarial organisms and the ameba of amebic dysentery, are much more sensitive to the lethal effects of high pressure oxygen than their host, this differential tolerance might conceivably have practical applications.

The effects of pure oxygen at pressures only slightly above 1 atmosphere have been investigated on human subjects by Demuth and Moschkowski (*1551*) 1927–28. Two persons were subjected to compressed oxygen in a chamber of 5,145 liters' capacity. For 20 minutes the subjects breathed oxygen at a pressure of 1 atmosphere. The pressure was then raised in 1 hour to 1.4 atmospheres and then up to 1.5 atmospheres for 3½ hours and returned to normal pressure again. Except for moderate pressure sensations in the ear which were easily dispersed, the subjects experienced no unfavorable symptoms, and the experiment was discontinued only because of exhaustion of the oxygen supply. There was

some fatigue toward the end. The temperature, pulse, and respiratory rate remained unchanged, and the systolic blood pressure was raised in one subject and fell in the other. The changes in both subjects were insignificant. There were no clear-cut alterations in the hemoglobin values or the red blood cell count. The urine indicated a tendency toward "alkalosis," there being a rise in the total titratable bases. The urine volume was increased, as well as the insensible body water loss.

Kimura, Suzuki, Moteki, Sugata, and Kawaai (*1555*) 1932 reviewed the effects of oxygen under pressures of 71 to 99 lb. in animals. The authors reported a reduction in serum albumin, no significant change in serum chlorides, a fall in the hemoglobin values and red blood cell count, a rise in the white blood cell count, irregular respirations with a fall in rate, a rise in respiratory volume, and a tendency to lung hemorrhages and congestion. There was apparently no significant change in the pulse rate. One-third of the animals died in convulsions. Oxygen convulsions were also considered by Garbarini (*1552*) 1943 and the reader is particularly referred to an important paper by Behnke, Johnson, Poppen, and Motley (*1548*) 1934–35 on the effect of oxygen on human subjects at pressures from 1 to 4 atmospheres. Subjects breathing oxygen through a mask at 1 atmosphere while at rest tolerated this exposure for 2 to 4 hours. One individual showed an increase in respiratory rate, and a rise in blood pressure and pulse after 3 hours. Three subjects breathing oxygen at a pressure of 2 atmospheres for 3 hours showed no ill effects, and four subjects were unharmed by breathing oxygen at 3 atmospheres for 2 hours. In another experiment, two subjects breathed oxygen under a pressure of 4 atmospheres for 45 minutes. In one, there was sudden blanching, sweating, and a fall in blood pressure. The other had a sudden convulsive seizure, first with tonic and then clonic movements. Both reactions supervened between the forty-third and forty-fourth minutes. There was complete recovery upon inhalation of air. In another group of experiments, the subjects breathed 97 percent oxygen at normal atmosphere pressure for 1 to 4 hours in the recumbent position. There was an increase in the leucocyte count after 4 hours in three out of six subjects. One individual developed dyspnea after 2 hours. After breathing pure oxygen at 1 atmosphere for 3 hours, there was an increase in blood pressure; and neuromuscular coordination, as measured by a pursuit meter, and attention demanded great effort. Oxygen was considered to act as a poison to the central nervous system, affecting neuromuscular coordination and causing convulsive seizures.

Behnke, Forbes, and Motley (*1547*) 1935–36 found that human subjects tolerated an oxygen pressure of 3 atmospheres for 3 hours without symptoms. After this time, further exposure to high oxygen pressure resulted in a contraction of the visual fields, dilatation of the pupils, and reduction of visual acuity. There was elevation of blood pressure, acceleration of the pulse, pallor, dizziness, and stupefaction.

For a further general consideration of the main features of oxygen poisoning at raised barometric pressures, the reader is referred to a report by Griffith and Schrenk (*1553*) published in 1940. This paper contains a review of previous work on the effects of breathing oxygen under pressure and describes tests carried out by the investigators on two healthy subjects, exercising vigorously and breathing oxygen at a pressure of 35 lb. or 3.4 atmospheres (absolute). The subjects were adversely affected in 36 and 31 minutes respectively. There were manifestations of motor incoordination, respiratory rate and force were increased, and there was some nausea and vomiting. These symptoms were attributed to oxygen poisoning; it was also considered that an increased concentration of carbon dioxide within the apparatus may have enhanced the toxic action of oxygen. These investigators concluded that the danger of breathing pure oxygen is increased rapidly at pressures in excess of 2 to 3 atmospheres (absolute). With regard to wearing an oxygen respirator under pressure, the authors saw no definite reason why such a respirator should not be worn, although none of the subjects was able to wear it while "going under"

pressure. The effect of raised barometric pressure on the life of the canisters was not studied. An increase in the resistance to inhalation while under increased pressure was observed, but apparently this caused serious discomfort in but one case.

1547. Behnke, A. R., H. S. Forbes, and E. P. Motley. Circulatory and visual effects of oxygen at 3 atmospheres pressure. *Amer. J. Physiol.*, 1935–36, *114:* 436–442. [P]

1548. Behnke, A. R., F. S. Johnson, J. R. Poppen, and E. P. Motley. The effect of oxygen on man at pressures from 1 to 4 atmospheres. *Amer. J. Physiol.*, 1934–35, *110:* 565–572. [P]

1549. Bornstein, A. and [ ] Stroink. Ueber Sauerstoffvergiftung. *Dtsch. med. Wschr.*, 1912, *38:* 1495–1497. [P]

1550. Cleveland, L. R. Toxicity of oxygen for protozoa in vivo and in vitro: animals defaunated without injury. *Biol. Bull. Wood's Hole*, 1925, *48:* 455–468. [P]

1551. Demuth, F. and S. Moschkowski. Beobachtungen über die Wirkung erhöhten Sauerstoffdruckes auf desunde Menschen. *Z. ges. exp. Med.*, 1927–28, *58:* 511–514. [P]

1552. Garbarini, G. Azione dell'alta tensione di ossigeno sull'organismo animale. *Fisiol. e. Med.*, 1934, *5:* 41–57.

1553. Griffith, F. E. and H. H. Schrenk. Use of respiratory protective devices under abnormal air pressure. *Rep. Invest. U. S. Bur. Min.*, 1940, no. 3488: 1–9. [P]

1554. Hill, L. and M. Greenwood, Jr. The influence of increased barometric pressure on man. No. 3. The possibility of oxygen bubbles being set free in the body. *Proc. roy. Soc.*, 1907. *B*, *79:* 284–287. [P]

1555. Kimura, R., K. Suzuki, K. Moteki, N. Sugata, and S. Kawaai. Experimental study on influence of concentrated oxygen gas by high pressure on human body. *Bull. nav. med. Ass. Japan*, 1932, *21*(3): (Japanese text pagination), 25–41; (English text pagination), 5-6. (In Japanese with English summary.)

1556. Phillipon, G. Action de l'oxygène et de l'air comprimés sur les animaux à sang chaud. *C. R. Acad. Sci., Paris*, 1893, *116:* 1154–1155. [P]

2. CONVULSIONS AND OTHER DISTURBANCES OF THE NEUROMUSCULAR MECHANISM

Convulsive manifestations due to oxygen poisoning have been carefully described in animals by Bert (*16*) 1878. This classical work contains a very complete bibliographical list of Bert's earlier reports. In 1873, Bert (*1563*) called attention to the similarity between oxygen convulsions and strychnine poisoning. Experimental animals became convulsed when the pressure reached about 3 atmospheres of oxygen. A review of Bert's work is also to be found in a report published in 1874 by Lépine (*1568*). It was recognized at that time that the oxygen tension and not the raised barometric pressure *per se* was the primary cause of the disturbance. It was also noted that raising the carbon dioxide concentration of the inspired gas mixture lowered the threshold for convulsions.

Lehmann (*1567*) 1883–84 disputed Paul Bert's interpretation of the convulsions associated with high oxygen pressure, and maintained that they were modified asphyxial seizures. In 1893, Foster (*1565*) summarized the existing knowledge of oxygen poisoning, calling attention to the fact that the threshold for the seizures in animals lay at approximately 3 atmospheres of oxygen or 15 atmospheres of air. They were considered to be similar to anoxic convulsions, and it was stated that plants, bacteria, and organized ferments are also destroyed by too great an oxygen pressure.

In 1933, Shilling and Adams (*1572*) published a careful study of convulsive seizures caused by breathing oxygen at high pressure. These investigations were conducted to estimate the danger of oxygen poisoning in escape from submarines with the aid of the submarine escape "lung." Mice were exposed to various oxygen tensions for 2-hour periods. No convulsions were observed unless the oxygen pressure rose above 35 lb. (gauge). Above 55 lb., all of the mice had convulsions. Similar results were obtained using guinea pigs and it was found that rabbits were more susceptible to oxygen convulsions than other laboratory animals. The onset of oxygen poisoning was always marked by irritation of the respiratory passages and disturbed breathing. At autopsy, there were congestior, edema, and hemorrhagic exudation in the lungs. No such pulmonary changes were observed in animals suffering from strychnine convulsions. It was concluded that breathing pure oxygen in the submarine escape "lung" would be dangerous if the "lung" were donned sometime before the actual escape.

Oxygen convulsions in rats were observed experimentally by Ozorio de Almeida (*1557*) 1934. He concluded that animals by repeated exposure become sensitized to the toxic action of oxygen. There is great individual variability in resistance to oxygen convulsions, and it was found that fasting increases the tolerance. At a pressure of 6 atmospheres of oxygen, rats which had been fed, had convulsions in 1 hour and 30 minutes; whereas, a rat after a 4-day fast, was well at the end of 5 hours and did not die until 6 hours and 48 minutes after the beginning of the exposure to the compressed oxygen. A rat which had not been fed for 6 days was able to tolerate an oxygen pressure of 6 atmospheres for 8 hours and 30 minutes. It was concluded that fasting prevents convulsions up to 6 atmospheres of oxygen, and that it delays pulmonary congestion. Ozorio de Almeida also called attention to the fact that atrophy of the testes resulted in male rats and that males suffered irreversible sterility. Mating was not, however, interfered with. Histological examination showed destruction of the seminal epithelium and other histological changes comparable to the histological picture produced by irradiation of the testes. In the female rat, the sterility persisted for several months, but established pregnancies were not interfered with by oxygen at high pressure.

Massart (*1569*) 1934 called attention to the role of carbon dioxide tension in oxygen poisoning. He concluded that factors tending to accelerate respiration increased the incidence of convulsions. In 1936 Prikladowizky (*1570*) investigated oxygen convulsions in experimental animals. Twelve- to thirteen-day-old mice exposed for periods up to 2 hours at oxygen pressures of 8 atmospheres suffered no typical convulsions, and survived longer than adult mice. Twelve- to twenty-two-day-old mice behaved in high oxygen pressures like adults, but showed somewhat greater tolerance. At ages above 22 days, the symptoms were exactly the same as in adult animals. Intraperitoneal injections of a 1 to 2,000 solution of strychnine produced typical convulsions irrespective of age. The author found that the development of cortical excitability in young mice paralleled the susceptibility to oxygen at high pressures and concluded that the oxygen convulsions are due to the excitatory process within the cerebral cortex. In further experiments, Prikladovizky (*1571*) found that at an oxygen pressure of 3.3 atmospheres, white mice became convulsed in 77 minutes. At 4 atmospheres' oxygen pressure, convulsions began in 23 minutes, while at 5 atmospheres of oxygen, convulsions supervened in 18½ minutes. At 6 atmospheres, the convulsions began in 9½ minutes, and at 7 and 8 atmospheres, the animals became convulsed in 4.8 minutes. At oxygen pressures up to 3 atmospheres, there were no convulsive manifestations. In mice, cats, and rabbits, the first convulsions appeared between 3 and 4 atmospheres of oxygen.

In a study designed to investigate the mode and site of action of oxygen at increased barometric pressures on the mammalian organism, Bean and Rottschafer (*1558*) 1937 exposed decorticated dogs to oxygen at 3 to 5 atmospheres' pressure. The respiration was increased; there was dyspnea, a reduction in heart rate, a rise in blood pressure, and convulsions. Convulsions were not averted by denervation of the carotid sinus alone, vagal section alone, or vagal blockage after sinus denervation. It was suggested that oxygen at high pressure may paralyze normal vagal influences on the respiratory mechanism. Bean and Rottschafer (*1559*) in 1938–39 found that the slowing of the heart as a result of high oxygen pressure was much less pronounced in decerebrated and sinus-denervated dogs than in controls. There was some indication that intact vagus nerves tended to protect the organism against oxygen convulsions. After the convulsion, animals remain hyperexcitable for several days following return to normal air, according to Bean and Siegfried (*1560*) 1943. They also tend to show a change from a docile to a combative attitude.

Memory and retention are also affected by exposure to oxygen at high pressures, as experiments on rats by Bean, Wapner, and Siegfried (*1562*) 1934 have shown. Young adult albino rats were exposed to oxygen at pressures slightly over 5 atmospheres (absolute)

for 8 to 15 minutes in a series of 16 successive exposures over a period of 9 days with not more than 2 exposures per day. Precautions were taken to eliminate possible complications from high carbon dioxide content and from bubble formation on decompression. So far as possible, convulsions or neuromuscular disturbances were avoided. Tests for learning and memory were conducted on the Lashley maze, the criterion for having learned the maze being 10 error-free runs on each of 2 successive days. There was an interval of 1 day between the final exposure to high pressure oxygen and the testing of the animal on the maze. Control animals were treated in the same manner, except that they were not exposed to high oxygen pressure. There was no significant difference in the ability of the control and test rats to learn the maze in tests begun 1 day after the last of the series of oxygen exposures. However, mice who had previously mastered the maze and were then exposed to high oxygen pressure commonly refused to run the maze for some hours thereafter. Their performance continued to be adversely affected for several weeks. This disturbance of memory was not dependent upon the occurrence of convulsive attacks, either during the maintenance of high oxygen pressure or during decompression therefrom. It is thus seen that oxygen at raised pressures can adversely affect the higher functions of the central nervous system even though it may not induce obvious neuromuscular dysfunction.

Permanent motor disabilities may be induced by successive exposures to oxygen at high pressure, as Bean and Siegfried (*1561*) showed in 1945. Young albino rats were exposed to pure oxygen at a gauge pressure of 65 lb. for 10 to 25 minutes two to four times a day until a desired severity of chronic disability was induced. Carbon dioxide was absorbed from the chamber as it was produced and, so far as possible, the occurrence of convulsive seizures was avoided. Decompression was carried out at a slow rate to reduce the likelihood of bubble formation. The acute reactions on return to normal air after single exposures varied. Usually, recovery took place within a few minutes or hours. On repeated exposure, there were chronic motor disabilities, such as spastic paralysis of the limbs, in some cases persisting as long as 18 months, when the animals were sacrificed. Eight-day-old chicks exposed to oxygen at pressures of 90 and 65 lb. gauge over several days also showed motor disabilities which persisted into adult life.

1557. Almeida, A. Ozorio de. Recherches sur l'action toxique des hautes pressions d'oxygène. *C. R. Soc. Biol. Paris*, 1934, *116:* 1225–1227. [P]

1558. Bean, J. W. and G. Rottschafer. The mode and site of action of oxygen at increased barometric pressures on the mammalian organism. *Amer. J. Physiol.* 1937, *119:* 268–269. [P]

1559. Bean, J. W. and G. Rottschafer. Reflexogenic and central structures in oxygen poisoning. *J. Physiol.*, 1938–39, *94:* 294–306. [P]

1560. Bean, J. W. and E. C. Siegfried. Residual effects of oxygen at high barometric pressure. *Fed. Proc. Amer. Soc. exp. Biol.*, 1943, *2:* 2. [P]

1561. Bean, J. W. and E. C. Siegfried. Permanent motor disabilities induced by successive exposures to oxygen at high pressures. *Fed. Proc. Amer. Soc. exp. Biol.*, 1945, *4:* 6. [P, M]

1562. Bean, J. W., S. Wapner and E. C. Siegfried. Residual disturbances in the higher functions of the C.N.S. induced by oxygen at high pressure. *Amer. J. Physiol.*, 1945, *143:* 206–213. [P]

1563. Bert, [ ]. Quelques nouveaux détails sur l'empoisonnement par l'oxygene. *Gaz. méd. Paris*, 1873, Sér. 4, *28:* 453–454. [C]

1564. Cohn, R. and I. Gersh. Changes in brain potentials during convulsions induced by oxygen under pressure. *J. Neurophysiol.*, 1945, *8:* 155–160. [P, M]

1565. Foster, M. *A text book of physiology.* London, MacMillan and Co., 1893, Sixth edition, 2 vols. [R]

1566. Herter, C. A. Notes on the toxic properties of the blood in epilepsy *J. nerv. ment. Dis.*, 1899, *26:* 72–83. [P]

1567. Lehmann, K. B. Über den Einfluss des comprimirten Sauerstoffs auf die Lebensprocesse der Kaltblüter and einige Oxydationsvorgänge. *Pflüg. Arch. ges. Physiol.*, 1883–84, *33:* 173–179. [P]

1568. Lépine, R. De l'influence de la pression barométrique sur les phénomènes vitaux. *Gaz. méd. Paris*, 1874, *45:* 285; 373–374. [R]

1569. Massart, L. Sur une prétendue relation entre l'oxydose et l'acidose gazeuse. *C. R. Soc. Biol. Paris*, 1934, *117:* 265–266. [P]

1570. Prikladowizky, S. I. Über die Natur der Krampfanfälle bei hohem Sauerstoffdruck bei Warmblütern. *Z. ges. exp. Med.*. 1936, *99:* 9–16. [P]

1571. Prikladovitsky, S. I. [Toxic effect of high oxygen pressure on the animal organism.] *Fisiol. Zh, S.S.S.R.*, 1936, *20:* 518–533. (With German summary.) [P]

1572. Shilling, C. W. and B. H. Adams. A study of convulsive seizures caused by breathing oxygen at high pressures. *Nav. med. Bull., Wash.*, 1933, *31:* 112–121. [P]

3. EFFECTS ON THE CARDIOVASCULAR SYSTEM

de Cyon (*1573*) in 1882 reported that in dogs the blood pressure falls as soon as the oxygen pressure reaches 1½ atmospheres. With pure oxygen there may be a rapid fall of blood pressure to shock levels at a pressure of 3 atmospheres. With air at 2 atmospheres, the pulse increases, but with pure oxygen at 2 atmospheres the pulse rate is doubled. The respiration becomes slow and shallow. Oxygen was not considered to be a specific poison for the organism, and death was ascribed to diminution in the carbon dioxide level resulting in reduced excitation of the vagal center. In contrast to the findings of de Cyon, experiments on human subjects breathing oxygen for 3½ hours at 1 to 1½ atmospheres, reported by Demuth and Moschkowski (*1574*) 1927–28, showed a rise in systolic blood pressure of 11 to 23 mm. Hg.

Bean (*1445*) has stated that the cardiovascular effects of breathing oxygen under high pressure will largely depend upon the general response of the animal to the high pressure. For example, the response of an animal in the convulsive stages of oxygen poisoning may be quite different from an animal which had not reached this stage; and it may be possible that the circulatory changes, occurring as a result of violent motor activity due to oxygen at high pressure, may mask some of the cardiovascular changes characteristic of the more immediate action of oxygen under high pressure. A review of the literature as cited by Bean indicates conflicting findings regarding changes in pulse rate and blood pressure. The effect of high oxygen pressure upon the caliber of blood vessels and volume flow of the blood is discussed by Bean.

1573. Cyon, E. de. L'action des hautes pressions atmosphériques sur l'organisme animal. *Paris méd.*, 1882, *7:* 158–159. [P]

1574. Demuth, F. and S. Moschkowski. Beobachtungen über die Wirkung erhöhten Sauerstoffdruckes auf gesunde Menschen. *Z. ges. exp. Med.*, 1927–28, *58:* 511–514. [P]

4. EFFECTS ON THE BLOOD

Guareschi (*1577*) 1933 found that white rats exposed to an oxygen pressure of 2 atmospheres for approximately 20 minutes showed no consistent effect on the white blood cell count or the differential count. In a paper by Bean and Haldi (*1575*) 1932, it was reported that in dogs exposed to high oxygen pressure, there was an increase in blood lactic acid. Behnke, Shaw, Shilling, Thomson, and Messer (*1576*) 1934 subjected dogs to oxygen at 3 to 3.89 atmospheres for 52 to 193 minutes. There was no change in the capacity of hemoglobin to take up oxygen or in the carbon dioxide carrying capacity of the blood. The pH was only 0.03 lower for 4 atmospheres of oxygen than for air. In two out of nine dogs, convulsions were observed. There was spasmodic respiration; pulmonary congestion and atelectasis were seen at autopsy. In a study of the effect of high oxygen pressure on various chemical constituents of the blood, Shilling, Thomson, Behnke, Shaw, and Messer (*1578*) 1934 reported that some dogs dying or having convulsions as a result of exposure to an oxygen pressure of 4 atmospheres showed increases in blood sugar and phosphorous content of the blood. In other animals, there were no changes in these constituents.

1575. Bean, J. W. and J. Haldi. Alternations in blood lactic acid as a result of exposure to high oxygen pressure. *Amer. J. Physiol.*, 1932, *102:* 439–447. [P]

1576. Behnke, A. R., L. A. Shaw, C. W. Shilling, R. M. Thomson, and A. C. Messer. Studies on the effects of high oxygen pressure. I. Effect of high oxygen pressure upon the carbon-dioxide and oxygen content, the acidity, and the carbon-dioxide combining power of the blood. *Amer. J. Physiol.*, 1934, *107:* 13–28. [P, R]

1577. Guareschi, G. Contributo allo studio della influenza delle alte pressioni nell'organismo. Influenza dell'ossigeno sotto pressione sulla formula leucocitaria. *Arch. Antrop. crim.*, 1933, *53:* 714–725. [P]

1578. Shilling, C. W., R. M. Thomson, A. R. Behnke, L. A. Shaw, and A. C. Messer. Studies on the effect of high oxygen pressure. II. Effect of high oxygen pressure on the sugar, phosphorus, non-protein nitrogen, chloride, creatinin, calcium and potassium content of the blood. *Amer. J. Physiol.*, 1934, *107:* 29–36. [P]

5. EFFECTS ON THE RESPIRATORY SYSTEM

Pathological effects on the respiratory system are produced not only by inhalation of oxygen or hyperoxygenated mixtures at normal atmospheric pressure, but also on breathing oxygen at a high tension, as Smith (*1585*) in 1898 pointed out. Mice which had breathed oxygen corresponding to 130 percent of 1 atmosphere contracted pneumonia in 08 hours. With pressure corresponding to 180 percent of 1 atmosphere, the pathological process supervened in 24 hours and in 5 hours at 300 percent. Mice showed signs of tetany on breathing oxygen corresponding to 450 percent of 1 atmosphere. Schmiedehausen (*1584*) 1909 found pathological lesions in the lungs of mice, rabbits, and guinea pigs that had breathed oxygen at pressures of 3 to 4 atmospheres. Schmidt and David (*1583*) 1912 subjected dogs and cats to an oxygen pressure of 1.2 atmospheres for 2 to 3 days. In these animals, no lung changes were seen. Bean (*1579*) 1931 reported the effects of breathing oxygen at pressures of 3 to 5 atmospheres on dogs. There was an increase in the respiratory minute volume, a diminution of oxygen absorption, and a tendency toward increased acidity of blood and tissues. There was a fall in the pulse rate. Bean (*1580*) 1932 found that exposure to oxygen at raised barometric pressures (up to 3,700 mm. Hg or 4.9 atmospheres) may give rise to periodic breathing and changes in the heart rate, blood pressure, and volume of blood flow. There were also changes in the oxygenation of the blood.

In mice exposed to an oxygen-hydrogen mixture at a pressure corresponding to 4 atmospheres of oxygen and 2 atmospheres of hydrogen, Libbrecht and Massart (*1582*) in 1934 observed no convulsions, but encountered pulmonary disturbances. Libbrecht and Massart concluded that the convulsions and pulmonary disturbances as symptoms of oxygen poisoning were two separate, unrelated phenomena. It is true that convulsions do occur in animals in which no changes have been observed in the lungs. However, one may conclude, with Bean (*1445*), that pulmonary pathology induced by oxygen at high pressure may contribute to the reactions of the organism in oxygen poisoning, possibly by interference with normal excretion of carbon dioxide. As Campbell (*1531*) 1929–30 has shown in rabbits breathing oxygen under a pressure of 3½ atmospheres, there is a definite increase in the oxygen and carbon dioxide tension in the tissues, and there is some evidence that the carbon dioxide tension may be increased to a dangerous level. It is possible also that pulmonary changes may result in anoxemia which may constitute a contributory factor in the genesis of convulsive seizures.

1579. Bean, J. W. Effects of high oxygen pressure on carbon dioxide transport, on blood and tissue acidity, and on oxygen consumption and pulmonary ventilation. *J. Physiol.*, 1931, *72:* 27–48. [P]

1580. Bean, J. W. Periodic ventilation as induced by exposure to high pressures of oxygen. *Amer. J. Physiol.*, 1932, *100:* 192–201. [P]

1581. Campbell, J. A. Effects of breathing oxygen at high pressures upon tissue gas tensions. *J. Physiol.*, 1929–30, *68:* vii-viiiP. [P]

1582. Libbrecht, W. and L. Massart. L'antagonisme oxygène-hydrogène. *C. R. Soc. Biol. Paris*, 1934, *117:* 264–265. [P]

1583. Schmidt, A. and O. David. Zur Frage der Sauerstoffvergiftung. *Dtsch. med. Wschr.*, 1912, *38:* 1697. [P]

1584. Schmiedehausen, G. *Die pathologisch-anatomischen Veränderungen der Lungen bei verändertem Sauerstoffgehalt der Atemluft.* Inaug.-Diss. (Med.) Halle, Wischan & Burkhardt, 1909, 20 pp. [P]

1585. Smith, J. L. The pathological effects of breathing oxygen at a high tension. *Brit. med. J.*, 1898, *2:* 610. [P]

6. EFFECTS ON METABOLISM

In general, the evidence from the literature indicates that oxygen at high pressure causes a decrease in metabolic rate. However, many reports on which this conclusion is based involve experimental animals in terminal states in which depressed metabolic rate might be considered a part of the general slowing of the vital processes before death. Bounhiol (*1586*) 1929 believed that the metabolic processes were accelerated by oxygen under high pressure, and he suggested that this, together with deficient removal of electrolytes, resulted in an excessive accumulation of metabolites which would eventually depress and limit

the vital metabolic reactions. According to Fontaine (*1590*) 1929, oxygen consumption in fish and crustacians was increased with an increase in pressure. However, Campbell (*1587*) 1937 showed that rats exposed to 6 atmospheres of oxygen for periods of approximately 30 minutes suffered a fall in body temperature including depression of metabolic rate. If the animals were maintained at a room temperature of 31°–35°C., only 1 out of 10 survived, whereas, at 21°–27°C., only 1 out of 10 succumbed. Campbell maintained that this fall in body temperature was a protective metabolic reaction against the poisonous effects of oxygen under high pressures. This investigator (*1588*) 1937 found that rats given thyroxin, dinitrophenol, adrenalin, pituitrin, insulin, or eserine with atropine showed an increased susceptibility to the poisonous effects of 6 atmospheres of oxygen. Thyroidectomy protected rats from oxygen poisoning when exposed to 6 atmospheres of oxygen at 33°C; 6 thyroidectomized rats all lived, while out of 10 control animals, 9 failed to survive. Campbell believed that oxygen poisoning was due to increased oxygenation in nerve cells, and that factors which artificially induced alterations in metabolism affected the response of nerve cells to oxygen at high pressure; factors which reduced the metabolic rate lowered the susceptibility of animals to oxygen poisoning and *vice versa*. In 1938, Campbell (*1589*) reported that animals were also protected against oxygen poisoning by removal of the hypophysis.

1586. Bounhiol, [ ]. Sur la respiration en milieux suroxygénés. *C. R. Acad. Sci., Paris*, 1929, *188:* 1340–1342.

1587. Campbell, J. A. Body temperature and oxygen poisoning. *J. Physiol.*, 1937, *89:* 17–18P. [P]

1588. Campbell, J. A. Oxygen poisoning and the thyroid gland. *J. Physiol.*, 1937, *90:* 91–92P. [P]

1589. Campbell, J. A. Effects of oxygen pressure as influenced by external temperature, hormones and drugs. *J. Physiol.*, 1938, *92:* 29–31P. [P]

1590. Fontaine, M. De l'augmentation de la consommation d'O des animaux marins sous l'influence des fortes pressions. Ses variations en fonction de l'intensité de la compression. *C. R. Acad. Sci., Paris*, 1929, *188:* 460–461.

7. EFFECTS ON MUSCULAR CONTRACTION

Gréhant and Quinquaud (*1598*) reported in 1891 that muscle power in dogs was reduced by oxygen poisoning. Myographic recordings were taken of the contractions of the gastrocnemius muscle in dogs under control conditions, and after subjecting the animals to 5 atmospheres of oxygen for 20 minutes. These animals had convulsions both during the maintenance of pressure and on decompression, and the responses of the gastrocnemius muscle to galvanic stimuli were diminished by exposure to oxygen under high pressure. Isolated, striated muscle is also affected by oxygen under high pressure, as Bean and Bohr (*1591, 1592*) 1938 have shown. These investigators subjected isolated frog muscle preparations to an oxygen pressure of 5 atmospheres. There was an initial increase in the height of contraction elicited by stimulating the preparation directly or through the nerve. This was followed by a slower progressive decrease in the height of contraction. Apparently, the nerve fibers and myoneural junctions are no more profoundly affected by high oxygen tensions than the muscle itself. The toxic action of oxygen under high pressure was attributed to its poisoning effect on muscle enzymes.

Bohr and Bean (*1596*) 1939 exposed isolated frog hearts to high pressures of oxygen. It was found that at an oxygen pressure of 70 to 80 lb. gauge, there was an initial increase in the force of ventricular contraction, followed by a delayed and slight decrease. There was a delayed slowing in the frequency of the isolated heart and finally a cessation of automaticity. The conductivity of excised hearts was initially enhanced.

Mammalian smooth muscle is also affected by oxygen at high barometric pressure. Bohr and Bean (*1597*) 1939 found a diminution in the amplitude of spontaneous contractions of isolated duodenum at an oxygen pressure of 75 lb. gauge. Contractions became irregular. On decompression, "tonus" returned, but there was not complete recovery of contractility. Similar results were obtained by these investigators in 1940 with strips of pyloric sphincter of the rabbit. In 1944, they (*1595*)

again noted that isolated strips of pyloric sphincter of the rabbit were depressed by oxygen at high pressures.

Observations of Bean and Bohr (*1593*) 1940 indicate irreversible decrease in "tonus" of sphincter and radial muscles exposed to oxygen at pressures of 5 to 6 atmospheres. In general, pupillary dilatation has been a common finding in animals exposed to oxygen at high pressures. (See, for example, Kodama (*1599*) 1937.)

1591. Bean, J. W. and D. F. Bohr. Effects of high oxygen pressure on isolated tissue. *Amer. J. Physiol.* 1938, *123:* 11–12. [P]

1592. Bean, J. W. and D. F. Bohr. High oxygen effects on isolated striated muscle. *Amer. J. Physiol.*, 1938, *124:* 576–582. [P]

1593. Bean, J. W. and D. F. Bohr. Sphincter and radial iris muscle reaction to high oxygen. *Amer. J. Physiol.*, 1940, *129:* 310. [P]

1594. Bean, J. W. and D. F. Bohr. Anoxic effects of high oxygen pressure on smooth muscle. *Amer. J. Physiol.*, 1940, *130:* 445–453. [P]

1595. Bean, J. W. and D. F. Bohr. The response of mammalian smooth muscle to oxygen at high pressure and its possible relationship to oxygen poisoning of respiratory enzyme systems. *Amer. J. Physiol.*, 1944, *142:* 379–390. [P]

1596. Bohr, D. F. and J. W. Bean. Oxygen poisoning in cardiac tissue. *Amer. J. Physiol.*, 1939, *126:* 188–195. [P]

1597. Bohr, D. F. and J. W. Bean. Effects of oxygen at high barometric pressure on some mammalian smooth muscle. *Amer. J. Physiol.*, 1939, *126:* P 437–438. [P]

1598. Gréhant, [ ] and [ ] Quinquaud. Mesure de la puissance musculaire dans l'empoisonnement par l'oxygène comprimé. *C. R. Soc. Biol. Paris*, 1891, Sér. 9, *3:* 417–418. [P]

1599. Kodama, S. Influence of high atmospheric pressure on the rabbit's eye. (After the experiment of K. Iwasaki). *Tohoku J. exp. Med.*, 1937, *31:* 357–374.

D. USES OF OXYGEN UNDER PRESSURE IN THERAPY

The reader should consult the section on the therapeutic effects of gases under raised atmospheric pressures (p. 302) for a consideration of the literature in this field. The therapeutic action of high oxygen pressure is discussed by Bean (*1445*) 1945 as applied to its use in decompression from compressed air to prevent the "bends," its effect on tumor growth, its uses in carbon monoxide poisoning, and its application in the treatment of shock. Mosso (*1603*) 1900 reported that dogs, rabbits, and monkeys were not poisoned by inhaling carbon monoxide if maintained under an oxygen pressure of 2 atmospheres or an air pressure of 10 atmospheres. Mosso suggested the use of oxygen under pressure in reviving miners and other individuals overcome by carbon monoxide poisoning.

Of considerable interest in connection with the role of high oxygen pressure in the production of convulsive seizures are the experiments conducted by Lennox and Behnke (*1601*) 1936. Three patients having many *petit mal* seizures were subjected to an oxygen pressure of 60 lb. or approximately 5 atmospheres (absolute). There was a decrease in the number of spontaneous seizures, and an increase in the degree of overventilation required to induce a seizure. In one patient in which the oxygen pressure was increased to 5 atmospheres (absolute), the lung ventilation required to produce a seizure was increased fivefold. An oxygen tension below normal tended to precipitate *petit mal* attacks.

A reference to the treatment of psoriasis with oxygen under pressure is contained in a report by de Mesquita (*1602*) 1941.

According to Frank and Fine (*1600*) 1943, exposure of animals to an oxygen pressure of 3 atmospheres did not favorably alter the survival time or the outcome in shock, and it was concluded that oxygen was of doubtful value as a therapeutic agent in hemorrhagic shock.

1600. Frank, H. A. and J. Fine. Traumatic shock. V. A study of the effect of oxygen on hemorrhagic shock. *J. clin. Invest.*, 1943, *22:* 305–314. [P]

1601. Lennox, W. G. and A. R. Behnke, Jr. Effect of increased oxygen pressure on the seizures of epilepsy. *Arch. Neurol. Psychiat., Chicago*, 1936, *35:* 782-788. [P]

1602. Mesquita, A. P. de. Tratamento da psoriasis pelo oxigenio sob pressão. *Brasil-med.*, 1941, *55:* 684–688.

1603. Mosso, A. Action physiologique et applications thérapeutiques de l'oxygène comprimé. *C. R. Acad. Sci., Paris*, 1900, *131:* 483–484. [P]

E. EFFECT OF OXYGEN ON TUMOR GROWTH

High oxygen tensions have been shown to have a destructive action on atypical cells,

although this action has not yet found effective application in the treatment of malignant tumors. Burrows (*1607*) 1917 found that variations in oxygen tension affected the growth of cultures of chick embryonic tissue. Good growth was observed until the oxygen percentage supplied to the cultures fell to 7 percent. There was some growth at a 6 percent oxygen concentration. The cells grew well in pure oxygen at 1 atmosphere. Actually, the growth at concentrations of 90 to 100 percent was more rapid but no more luxuriant than at 9 to 10 percent concentrations. Fischer and Andersen (*1610*, *1611*) 1926 found that the cells of some tumors were more susceptible to the destructive action of oxygen at high pressure than were normal cells. Rous' sarcoma was destroyed in approximately 1 to 30 hours by the action of oxygen under pressures of 1 to 6 atmospheres. The cure was not always complete, but some benefit was always observed (*1610*). It was found that if copper or selenium was injected prior to subjecting the animals to high pressure oxygen, the lethal action on the tumor cells, as compared with the effect on normal cells, was more pronounced.

Fischer, Andersen, Demuth, and Laser (*1613*) 1926–27 treated mice having carcinoma with oxygen under pressure. The animals were subjected to either 1.6 atmospheres for 20 to 22 hours, or 2 atmospheres for 14 hours. The pressure was increased to the desired level in 15 to 30 minutes and decompression occupied 1 to 1½ hours. The amount of pressure and duration were governed by the capacity of the mice to withstand pneumonia. Only 2 percent of the mice treated by oxygen alone showed recovery; whereas, 21 out of 141 or 15 percent of the mice treated by intravenous injection of a glucose-copper preparation were healed. Attempts to use high oxygen pressure in the treatment of malignant disease in man by Auler, Herzogenrath, and Wolff (*1605*) 1929 failed to attain any real degree of success. Ozorio de Almeida (*1604*) 1934 found that previous starving of rats enhanced the selective destructive action of high oxygen pressure upon sarcoma cells. Normal cells became more resistant, whereas, the malignant cells were more completely destroyed.

Basset, Wollman, Macheboeuf, and Bardach (*1606*) 1935 reported that mouse sarcoma "37," bathed in physiological saline solution, was destroyed by exposure to oxygen at a hydrostatic pressure of 1,800 atmospheres for 30 minutes, but that it was unaffected by a pressure of 1,000 atmospheres.

Campbell (*1608*) in 1933 failed to demonstrate any effect on the development of tar cancer in mice breathing 60 percent oxygen, and in 1937 (*1609*) reported no retarding action on tumor growth in mice with sarcoma transplants exposed to oxygen at 6 atmospheres for 1 hour a week for 7 weeks. Rats exposed once a week for 7 weeks to an oxygen pressure of 5 atmospheres also showed no retardation of tumor growth. Twenty percent of the animals used in the latter experiment died from the experimental procedure.

1604. Almeida, A. Ozorio de. Traitement et guérison, par l'oxygène, du cancer expérimental des rats. *C. R. Soc. Biol. Paris*, 1934, *116:* 1228–1230. [P]

1605. Auler, H., H. Herzogenrath, and B. Wolff. Beiträge zur Frage der O_2—überdrucktherapie beim krebskranken Menschen. *Z. Krebsforsch.*, 1929, *28:* 466–489. [P]

1606. Basset, J., E. Wollman, M.-A. Macheboeuf, and M. Bardach. Études sur les effets biologiques des ultrapressions: action des pressions élevées sur les tumeurs. *C. R. Acad. Sci., Paris*, 1935, *200:* 1247–1248. [P]

1607. Burrows, M. T. The oxygen pressure necessary for tissue activity. *Amer. J. Physiol.*, 1917, *43:* 13–21.

1608. Campbell, J. A. The influences of breathing carbon monoxide and oxygen at high percentages for prolonged periods upon development of tar cancer in mice. *J. Path. Bact.*, 1933, *36:* 243–248. [P]

1609. Campbell, J. A. Oxygen poisoning and tumour growth. *Brit. J. exp. Path.*, 1937, *18:* 191–197. [P]

1610. Fischer, A. and E. Buch Andersen. Über das Wachstum von normalen und bösartigen Gewebezellen unter erhöhten Sauerstoffdruck. *Skand. Arch. Physiol.*, 1926, *49:* 126–127.

1611. Fischer, A. and E. B. Andersen. Über das Wachstum von normalen und bösartigen Gewebezellen unter erhöhtem Sauerstoffdruck. *Z. Krebsforsch.*, 1926, *23:* 12–27.

1612. Fischer, A., E. B. Andersen, and F. Demuth. Untersuchungen über den Einfluss erhöhten Sauerstoffdruckes auf Mäusecarcinom in vivo. *Naturwissenschaften*, 1926, *14:* 1181.

1613. Fischer, A., E. B. Andersen, F. Demuth, and H. Laser. Untersuchungen über den Einfluss erhöhten Sauerstoffdruckes auf Mäusecarcinom in vivo. *Z. Krebsforsch.*, 1926–27, *24:* 528–562.

F. EFFECT OF HIGH OXYGEN TENSIONS ON BACTERIAL GROWTH

Paul Bert (*16*) 1878 reported that the micro-organisms responsible for the souring of wine were killed by oxygen-rich air at a pressure of 10 atmospheres and claimed that putrefactive processes were inhibited. He also maintained that oxygen under high pressure destroyed the organisms present in milk. Investigative work on the effects of high oxygen tension on bacterial growth has not confirmed all of Bert's conclusions, but there is clear evidence that many micro-organisms are deleteriously affected by oxygen at raised atmospheric pressure. Moore and Williams (*1617*) in 1909, for example, reported that the growth of the tubercle bacillus was inhibited by exposure to oxygen at a partial pressure corresponding to 0.8 and 0.9 atmospheres. On the other hand, the colon bacillus grew well under these conditions, while *Staphylococcus albus* was inhibited. Most of the Staphylococci were inhibited, while most of the typhosa group, except *Bacillus dysenteriae*, grew well on exposure to high oxygen percentages. In 1910–11, Moore and Williams (*1618*) investigated the comparative growth in air and in oxygen-rich mixtures of 26 different organisms. The tubercle bacillus and plague bacillus were both found to be oxyphobic. The former was killed in 3 weeks by oxygen percentages greater than 20 percent, whereas, the latter was inhibited by 60 to 90 percent oxygen concentrations in 3 days. The Staphylococci were somewhat inhibited, while other organisms showed no ill effects. Adams (*1614*) 1912 also found that atmospheres enriched with oxygen inhibited the growth of bacterial cultures but reported no improvement in patients suffering with pulmonary tuberculosis upon inhalation of 80 percent oxygen.

Karsner, Brittingham, and Richardson (*1616*) 1923–24 reported that 83 to 99 percent oxygen at normal atmospheric pressure inhibited the growth of *Proteus vulgaris*, *Streptococcus hemolyticus* and other organisms. Pigment formation by *Bacillus pyocyaneous* was inhibited. The pneumococcus was not inhibited. Thaysen (*1622*) in 1934 reported retardation of growth on exposing *Bacillus coli* and other micro-organisms to oxygen at a pressure of 10 atmospheres. The temperature was found to be a critical factor. Schlayer (*1621*) observed that the growth processes of type I pneumococcus depended upon the oxygen tension. Bean (*1615*) 1941 reported that the growth of pneumococcus type I was completely inhibited by oxygen pressure of 900 mm. Hg and that an oxygen pressure of 4,600 mm. Hg destroyed the organisms. Air pressures of 4,600 mm. Hg did not affect the organisms. For information as to the effect of oxygen under pressure on *Clostridium welchii*, the reader should consult a paper published in 1941 by Pacheco and Costa (*1620*). Reference should also be made to the review by Bean (*1445*). As he points out, the action of oxygen at high pressure on micro-organisms indicates that oxygen poisoning is not limited to the higher organisms or animals possessing red blood corpuscles and a cardiovascular system. Bean also concludes that in the lower forms of life, as well as in the higher, there is a considerable variation in susceptibility to oxygen poisoning. Such variations may be due, in part, to differences in structural characteristics and in the respiratory enzyme system.

1614. Adams, A. The effects of atmospheres enriched with oxygen upon living organisms, (*a*) effects upon micro-organisms, (*b*) effects upon mammals experimentally inoculated with tuberculosis, (*c*) effects upon the lungs of mammals, or oxygen pneumonia. *Biochem. J.*, 1912, *6:* 297–314.

1615. Bean, J. W. Oxygen poisoning of unicellular organisms and its relation to mammalian tissues. *Amer. J. Physiol.*, 1941, *133:* 208. [P]

1616. Karsner, H. T., H. H. Brittingham, and M. L. Richardson. Influence of high partial pressures of oxygen upon bacterial cultures. *J. med. Res.*, 1923–24, *44:* 83–88.

1617. Moore, B. and R. S. Williams. The growth of the *Bacillus tuberculosis* and other micro-organisms in different percentages of oxygen. *Biochem. J.*, 1909, *4:* 177–190.

1618. Moore, B. and R. S. Williams. The growth of various species of bacteria and other micro-organisms in atmospheres enriched with oxygen. *Biochem. J.*, 1910–11, *5:* 181–187.

1619. Novy, F. G. and M. H. Soule. Microbic respiration. II. Respiration of the tubercle bacillus. *J. infect. Dis.*, 1925, *36:* 168–232.

1620. Pacheco, G. and G. A. Costa. Influencia do oxigenio sob pressão sobre o "Clostridium welchii". *Rev. brasil. Biol.*, 1941, *1:* 145–153.

1621. Schlayer, C. The influence of oxygen tension in the respiration of pneumococci (type 1). *J. Bact.*, 1936, *31:* 181–189.

1622. Thaysen, A. C. Preliminary note on the action of gases under pressure on the growth of micro-organisms. I. Action of oxygen under pressure at various temperatures. *Biochem. J.*, 1934, *28:* 1330–1335.

G. EFFECT OF CARBON DIOXIDE IN THE PRODUCTION OF OXYGEN POISONING

A number of reports indicate that carbon dioxide plays a role in oxygen poisoning. For example, Shaw, Behnke, and Messer (*1624*) 1934 reported that high carbon dioxide tension increases the toxicity of raised oxygen pressures, and that carbon dioxide tensions which are harmless at an oxygen pressure of 1 atmosphere are highly toxic at 4 atmospheres of oxygen. Anesthetized dogs subjected to oxygen pressures up to 4 atmospheres (absolute), showed a fall in blood pressure and had convulsions. Reduction of the oxygen pressure led to remission of the symptoms. In such experiments, death may result from paralysis of either the respiratory or cardiovascular centers. Exposure to oxygen at a pressure of 3,031 mm. Hg plus carbon dioxide at 26 mm. Hg resulted in no convulsions; whereas, an oxygen-carbon dioxide mixture containing oxygen at a pressure of 2,935 mm. Hg and carbon dioxide at a pressure of 60 mm. Hg led to convulsive seizures within 57 minutes. Nonreduction of oxyhemoglobin in the absence of other changes, according to Bean (*1445*) 1945, provides sufficient explanation for the increased carbon dioxide tissue tension reported in oxygen poisoning, and there appears justification for Hill's conclusion (*1623*) 1933 that increased carbon dioxide tension is a factor in the production of high oxygen pressure convulsions.

1623. Hill, L. The influence of carbon dioxide in the production of oxygen poisoning. *Quart. J. exp. Physiol.*, 1933, *23:* 49–50. [P]

1624. Shaw, L. A., A. R. Behnke, and A. C. Messer. The rôle of carbon dioxide in producing the symptoms of oxygen poisoning. *Amer. J. Physiol.*, 1934, 108: 652–661. [P]

H. EFFECT OF HIGH OXYGEN TENSIONS ON ENZYME ACTIVITY

It has been suggested that the poisonous effects of increased oxygen tension are due to inactivation of enzyme systems. This literature is discussed by Bean (*1445*), whose review should be consulted. Reference should also be made to the work of Bert (*16*) 1878. In 1873, Bert (*1628*) reported that oxygen at high pressures arrested the fermentation of wine and inhibited the putrefaction of urine, and in 1875 (*1629*), he reported that oxygen pressures corresponding to 23 atmospheres of air prevented the spoiling of meat. Laqueur (*1644*) 1912 found that carbon dioxide and nitrogen increased the autolytic action of liver cells, and that oxygen at a pressure of 11.5 atmospheres caused a partial inhibition of this action. McCance (*1652*, *1653*) 1924 and 1925 reported that urea formation by autolysis of the cells of the spleen was inhibited by oxygen, and that this effect was largely reversible. He stated that oxygen acts only upon the enzymes and not upon the substrate.

Meyer (*1654*) 1927 reported that blood exposed to carbon monoxide loses its power to turn guaiacum blue with the normal amount of hydrogen peroxide. More peroxide than usual must be added. However, carbon monoxide does not affect the ability of muscle tissue to give the guaiacum reaction. Brain tissue that has been exposed to oxygen at a pressure of 4 atmospheres was found to be less efficient in the guaiacum reaction than unoxygenated brain tissue. Such tissue, when exposed to normal air in aqueous suspension, gradually increases in its ability to affect guaiacum. According to Salaskin and Solowjew (*1657*) 1931, oxygen decreases the activity of arginase, while cystein can reactivate arginase that has been saturated with oxygen. Bubbling oxygen through the enzyme while the cystein is being added, prevents the activation of the arginase by the latter. Edlbacher, Kraus, and Walter (*1631*) 1932 reported that at 40° C., oxygen inactivates preparations of arginase, reducing

its activity to one-third the original value. Edlbacher, Kraus, and Leuthardt (*1632*) 1933 found that arginase is irreversibly inactivated by oxygen. At a pH of 6 or less, this effect is diminished and finally disappears at a pH of 5. Glycerine, nitrogen, hydrogen, and carbon dioxide protect the enzyme against this effect of oxygen. In the tissues, sulfhydryl compounds act as oxygen acceptors, protecting the arginase from oxygen.

Hellerman, Perkins, and Clark (*1637*) 1933 found that aeration for 2½ to 3½ hours reduced urease activity by about 10 percent and that the activity was restored by cyanides or hydrogen sulfide. Marks (*1648*, *1649*) 1934 and 1935 and Marks and Fox (*1650*) 1933 reported that catalases from certain marine plants and animals were inactivated directly or indirectly by oxygen. According to Jowett and Quastel (*1643*) 1934, oxygen partially inhibits glyoxalase activity in most tissues. From investigations reported by Lehmann (*1645*) in 1935, it was concluded that at a critical pH value of about 7.4, oxygen at high tensions has an inhibiting action on succinic acid oxidation. Lehmann (*1645*) 1935 found that this inhibition is irreversible. Libbrecht and Massart (*1646*) 1935 observed that oxygen at pressures of 4 to 10 atmospheres altered the ratio between oxidized glutathione and reduced glutathione in rabbit's blood *in vitro*. In rabbits subjected to 4 atmospheres of oxygen for 30 minutes, the glutathione was nearly all reduced. It was, therefore, concluded that high tensions of oxygen diminished tissue oxidation.

According to Libbrecht and Massart (*1647*) 1937, the succinodehydrogenase reaction is also blocked. Succinic dehydrogenase is also inactivated by exposure to the oxidizing influence of oxidized glutathione. Hopkins, Morgan, and Lutwak-Mann (*1640*) 1938 reported that succinic dehydrogenase was also inactivated by alloxan, copper, and maleic and iodoacetic acids. Malonic, succinic, and fumeric acids protect succinic dehydrogenase from the influence of oxidized glutathione. These experiments, according to the investigators, support the view that succinic dehydrogenase depends for its activity upon the integrity of –SH groups in its structure. Bohr and Bean (*1630*) 1940–41 reported that exposure of succinic dehydrogenase extract from pork hearts for 2 hours to a pressure of 100 lb. resulted in a decrease in the enzyme activity of 9 to 50 percent. The process appeared to be irreversible.

According to Albaum, Donnelly, and Korkes (*1625*) 1942, exposure of grains of oats to pure oxygen at normal atmospheric pressure during the soaking period inhibits subsequent growth almost completely as compared with aerated controls. Enzyme assays carried out on extracts 30 hours after oxygenation indicated little or no change in cytochrome oxidase activity but there was a definitely lowered catalase activity and lowered endogenous dehydrogenase activity. In the course of normal development, nitrogen moves from the endosperm into the embryo. However, in plants grown from oxygenated grains, the nitrogen increase in the embryo occurs more slowly for a time and then stops. In the case of catalase, it was shown that oxygenation first slows down the activity of this enzyme and later causes its destruction. In plants grown from oxygenated grains, the amino nitrogen is lower in the embryo and in the endosperm, suggesting that high oxygen tension may interfere with proteolytic breakdown in the endosperm and consequently prevent nitrogen transport, the development of enzyme activity, and finally growth.

According to Potter and DuBois (*1655*) 1942–43, succinic dehydrogenase is inhibited by a large number of compounds whose only common denominator appears to be their ability to react with –SH groups. According to Barron and Singer (*1627*) 1943, glutathione protects –SH groups in their reduced form, maintaining them for enzyme activity dependent upon such groups.

For other studies relating to the role of oxygen in enzyme systems, reports by the following authors may be consulted: Wieland (*1665*) 1922; Stephenson and Stickland (*1661*) 1931; Edlbacher and Schuler (*1633*) 1932; Voegtlin and Maver (*1663*) 1932; Massart (*1651*) 1936; Hellerman (*1636*) 1937; Gale (*1635*) 1939; Gaffron (*1634*) 1940; Irving, Fruton, and Bergmann (*1641*, *1642*) 1941 and 1942; Sizer and Tytell (*1660*) 1941; Sizer

(*1659*) 1941–42; Rahn and Richardson (*1656*) 1942; Hoberman and Rittenberg (*1638*) 1943; Shapiro and Wertheimer (*1658*) 1943; and Warburg and Christian (*1664*) 1943.

1625. Albaum, H. G., J. Donnelly, and S. Korkes. The growth and metabolism of oat seedlings after seed exposure to oxygen. *Amer. J. Bot.*, 1942, *29:* 388–395.

1626. Bailey, B., S. Belfer, H. Eder, and H. C. Bradley. Oxidation, reduction, and sulfhydryl in autolysis. *J. biol. Chem.*, 1942, *143:* 721–728.

1627. Barron, E. S. G. and T. P. Singer. Enzyme systems containing active sulfhydryl groups. The role of glutathione. *Science*, 1943, *97:* 356–358.

1628. Bert, [ ]. Le résultat de récentes recherches sur l'action de l'oxygène comprimé sur les phénomènes nutritifs et de fermentation. *C. R. Soc. Biol. Paris*, 1873, Sér. 5, *5:* 381–382. [C, P]

1629. Bert, P. Influence de l'air comprimé sur les fermentations. *C. R. Acad. Sci., Paris.* 1875, *80:* 1579–1582. [C, P]

1630. Bohr, D. F. and J. W. Bean. Dehydrogenase inactivation in oxygen poisoning. *Amer. J. Physiol.*, 1940–41, *131:* 388–393.

1631. Edlbacher, S., J. Kraus, and G. Walter. Beiträge zur Kenntnis der Arginase. 7. Mitteilung. Aktivierungs- und Hemmungsversuche. *Hoppe-Seyl. Z.*, 1932, *206:* 65–77.

1632. Edlbacher, S., J. Kraus, and F. Leuthardt. Die Steureung der Arginasewirkung durch Sauerstoff. 9. Mitteilung zur Kenntnis der Arginase. *Hoppe-Seyl. Z.*, 1933, *217:* 89–104.

1633. Edlbacher, S. and B. Schuler. Zur Kenntnis der Arginasewirkung 8. Mitteilung. Thyroxin und Argininstoffwechsel. *Hoppe-Seyl. Z.*, 1932, *206:* 78–84.

1634. Gaffron, H. The oxyhydrogen reaction in green algae and the reduction of carbon dioxide in the dark. *Science*, 1940, *91:* 529–530.

1635. Gale, E. F. Formic dehydrogenase of *Bacterium coli:* its inactivation by oxygen and its protection in the bacterial cell. *Biochem. J.*, 1939, *33:* 1012–1027.

1636. Hellerman, L. Reversible inactivations of certain hydrolytic enzymes. *Physiol. Rev.*, 1937, *17:* 454–484.

1637. Hellerman, L., M. E. Perkins, and W. M. Clark. Urease activity as influenced by oxidation and reduction. *Proc. nat. Acad. Sci., Wash.*, 1933, *19:* 855–860.

1638. Hoberman, H. D. and D. Rittenberg. Biological catalysis of the exchange reaction between water and hydrogen. *J. biol. Chem.*, 1943, *147:* 211–227.

1639. Hopkins, F. G. and E. J. Morgan. The influence of thiol-groups in the activity of dehydrogenases. *Biochem. J.*, 1938, *32:* 611–620.

1640. Hopkins, F. G., E. J. Morgan, and C. Lutwak-Mann. The influence of thiol groups in the activity of dehydrogenases. II. With an addendum on the location of dehydrogenases in muscle. *Biochem. J.*, 1938, *32:* 1829–1848.

1641. Irving, G. W., Jr., J. S. Fruton, and M. Bergmann. The activation of intracellular proteinases. *J. biol. Chem.*, 1941, *139:* 569–582.

1642. Irving, G. W., Jr., J. S. Fruton, and M. Bergmann. On the proteolytic enzymes of animal tissues. IV. Differences between aerobic and anerobic proteolysis. *J. biol. Chem.*, 1942, *144:* 161–168.

1643. Jowett, M. and J. H. Quastel. The glyoxalase activity of tissues. *Biochem. J.*, 1934, *28:* 162–172.

1644. Laqueur, E. Über den Einfluss von Gasen, im besonderen von Sauerstoff und Kohlensäure, auf die Autolyse. V. Mitteilung. Autolyse und Stoffwechel. *Hoppe-Seyl. Z.*, 1912, *79:* 82–129.

1645. Lehmann, J. Über den Sauerstoffverbrauch bei der vitalen Bernsteinsäureoxydation in Abhängigkeit von Ph und Sauerstoffdruck. Ein Beitrag zur Kenntnis der toxischen Wirkung von Sauerstoff. *Skand. Arch. Physiol.*, 1935, *72:* 78–91.

1646. Libbrecht, W. and L. Massart. Le rapport glutathion oxydé/glutathion réduit lors de l'oxydose aiguë *C. R. Soc. Biol. Paris*, 1935, *120:* 1330.

1647. Libbrecht, W. and L. Massart. Influence de l'oxygène sous pression sur la succinodéhydrogénase. *C. R. Soc. Biol. Paris*, 1937, *124:* 299–300.

1648. Marks, G. W. The inactivation of catalases from certain marine animals by oxygen. *J. biol. Chem.*, 1934, *105:* 489-500.

1649. Marks, G. W. The inactivation of catalases from certain marine plants by oxygen. *Biochem. J.*, 1935, *29:* 509–512.

1650. Marks, G. W. and D. L. Fox. The inactivation of mussel catalase by oxygen. *J. biol. Chem.*, 1933, *103:* 269–283.

1651.* Massart, L. L'oxydose et le cytochrome. *Arch. int. Pharmacodyn.*, 1936, *53:* 562–568.

1652. McCance, R. A. The production of ammonia and urea in autolysis. *Biochem. J.*, 1924, *18:* 486–497.

1653. McCance, R. A. The influence of oxygen on the production of urea by enzymes of the liver and spleen. *Biochem. J.*, 1925, *19:* 134–140.

1654. Meyer, A. L. The effect of carbon monoxid and oxygen at high pressure on the power of animal tissue to cause the oxidation of guaiacum. *Amer. J. Physiol.*, 1927, *82:* 370–375.

1655. Potter, V. R. and K. P. DuBois. Studies on the mechanism of hydrogen transport in animal tissues. VI. Inhibitor studies with succinic dehydrogenase. *J. gen. Physiol.*, 1942–43, *26:* 391–404.

1656. Rahn, O. and G. L. Richardson. Oxygen demand and oxygen supply. V. The multiplication curve. *J. Bact.*, 1942, *44:* 321–332.

1657. Salaskin, S. and L. Solowjew. Über Beeinflussung der Arginase durch Sauerstoff, Kohlensäure und Zystein. Vorläufige Mitteilung. *Hoppe-Seyl. Z.*, 1931, *200:* 259–260.

1658. Shapiro, B. and E. Wertheimer. Fatty acid dehydrogenase in adipose tissue. *Biochem. J.*, 1943, *37:* 102–104.

1659. Sizer, I. W. The activity of yeast invertase as a function of oxidation-reduction potential. *J. gen. Physiol.*, 1941-42, *25:* 399–409.

1660. Sizer, I. W. and A. A. Tytell. The activity of crystalline urease as a function of oxidation-reduction potential. *J. biol. Chem.*, 1941, *138:* 631–642.

1661. Stephenson, M. and L. H. Stickland. Hydrogenase: a bacterial enzyme activating molecular hydrogen. I. The properties of the enzyme. *Biochem. J.*, 1931, *25:* 205-214.

1662. Trécul, [ ]. [Discussion of M. Bert's communication.] *C. R. Acad. Sci., Paris*, 1875, *80:* 1582. [C]

1663. Voegtlin, C. and M. E. Maver. Relation of oxidation to proteolysis in malignant tumors. *Publ. Hlth. Rep., Wash.*, 1932, *47:* 711–725.

1664. Warburg, O. and W. Christian. Isolierung und Kristallisation des Gärungsferments Zymohexase. *Biochem. Z.*, 1943, *314:* 149–176.

1665. Wieland, H. Über den Mechanismus der Oxydationsvorgänge. *Ergebn. Physiol.*, 1922, *20:* 477–518.

I. MECHANISM OF THE POISONOUS ACTION OF OXYGEN

Various factors which may play a part in the etiology of oxygen poisoning have been discussed by Bean (*1445*) 1945. Regarding pulmonary pathology as an etiological factor, Bean concludes that such pathology does contribute to the reactions which characterize oxygen poisoning. In animals this may, according to Bean, cause interference with the normal removal of carbon dioxide. During decompression and in the post-decompression period, those reactions which represent a persistence of the toxic effects of high oxygen pressure induced during the maintenance of increased pressure are further complicated by the pulmonary pathology which, when the animals return to normal pressure conditions, results in anoxemia. It has been amply shown that manifestations of oxygen poisoning can occur without damage to the lungs, so that, while pulmonary pathology, when present, is contributory thereto, it is not essential to the induction of oxygen poisoning.

Regarding the central nervous system as the site of origin of the reactions to oxygen at high pressure, Paul Bert (*1667*) 1873 stated that oxygen killed not by its effect on the red blood cells but had a direct action on the central nervous system. Bean (*1445*) 1945, in summarizing the literature on this subject, concluded that whether oxygen at high pressure operated directly upon the central nervous system or through the production of some intermediary toxic substance, or through a disturbed metabolism and removal of metabolites, or through a combination of these mechanisms acting on peripheral or central structures, the permanently crippling motor disturbances which can be induced by repeated exposure to high pressure oxygen offer satisfactory evidence that oxygen at raised pressures can cause irreversible damage to the central nervous system.

The role of carbon dioxide as an etiological factor has been discussed on page 190 and Bean's comment (*1445*) supports the conclusion that exposure to high oxygen pressure results in an increase in carbon dioxide tension in the tissues. As has been said, nonreduction of hemoglobin has been referred to in explanation of the increased carbon dioxide tension. Although the increase in carbon dioxide tension appears to be slight, nevertheless, a small increase in carbon dioxide becomes highly significant in the presence of high pressures. As a whole, it appears to Bean that increased carbon dioxide tension constitutes an important etiological factor in oxygen poisoning. On the other hand, carbon dioxide and its disturbed transport by the blood cannot be selected as the only causative factor. Probably, increased tissue acidity as a factor in oxygen poisoning is also of significance.

There may be definite disturbances of metabolism as a result of exposure to high oxygen tensions and the evidence, taken as a whole, indicates that high oxygen pressure does have a depressant action on the metabolic processes. According to Campbell (*1609*) 1937, the fall in body temperature associated with high oxygen tensions is a protective reaction, and Ozorio de Almeida (*1604*) 1934 considered

that the fall in metabolism was the cause of pulmonary damage and the convulsions of oxygen poisoning. Paul Bert (*16*) 1878 held that the fall in metabolism represented the actual death of cells and postulated the liberation of some toxic substance. However, Bean (*1445*) 1945 did not consider it necessary to resort to the theory of the formation of a hypothetical toxic substance.

As has been seen, oxygen under high pressure adversely affects enzyme mechanisms, and also kills or injures organisms depending for their life upon such enzyme reactions. The effect of oxygen at high pressure on enzyme activity probably constitutes an important factor in oxygen poisoning. According to Bean (*1445*), numerous observations support the view that in oxygen lack and in oxygen poisoning, the same fundamental processes are affected, and it is possible that the toxic action of oxygen under high pressure is due essentially to a condition of anoxia in the tissues. It has also been proposed that oxygen at high tensions may cause increased oxidation in the central nervous system, and that this may be a cause of oxygen poisoning. Bean considers, however, that augmentation of metabolism is not a characteristic response to high oxygen pressure.

Concerning Bert's theory that toxic substances may be liberated as a result of exposure to high oxygen tensions, Bean and Bohr (*1593*) 1940 were unable to demonstrate the release of any toxic substance from isolated smooth muscle poisoned by oxygen. Bean's discussion of the etiology of oxygen poisoning concluded with the statement that psychological factors may also play a role in determining the individual variations in tolerance to oxygen poisoning observed in human subjects. For other studies bearing on the mechanism of oxygen poisoning, the reader may refer to reports by the following authors: Bert (*1667*, *1668*, *1669*) 1873; Rosenthal (*1674*) 1902; Justin-Mueller (*1672*) 1918; Hubbs (*1671*) 1930; Brooks (*1670*) 1935; Barsoum and Gaddum (*1666*) 1935–36; and Prikladovizky (*1673*) 1942.

1666. Barsoum, G. S. and J. H. Gaddum. The effects of cutaneous burns on the blood histamine. *Clin. Sci.*, 1935–36, *2:* 357–362.

1667. Bert, [ ]. Expériences sur l'empoisonnement par l'oxygène. *Gaz. méd. Paris*, 1873, Sér. *4*, *28:* 387. [C, P]

1668. Bert, P. Le mode d'action de l'oxygène en excès dans le sang, mode d'action duquel résultent les convulsions et la mort. *C. R. Soc. Biol. Paris*, 1873, Sér. 5, *5:* 102–104. [C, P]

1669. Bert, [ ]. Sur les effets des modifications de la pression barométrique. *C. R. Soc. Biol. Paris*, 1873, Sér. 5, *5:* 262–264. [C, P]

1670. Brooks, J. The oxidation of haemoglobin to methaemoglobin by oxygen. II. The relation between the rate of oxidation and the partial pressure of oxygen. *Proc. roy. Soc.*, 1935, *B*, *118:* 560–577. [P]

1671. Hubbs, C. L. The high toxicity of nascent oxygen. *Physiol. Zoöl.*, 1930, *3:* 441–460. [P]

1672. Justin-Mueller, E. Contribution à la théorie de la transmission d'oxygène. *J. Pharm. Chim., Paris*, 1918, Ser. 7, *18:* 17–18. [P]

1673. Prikladovizky, S. I. (The mechanism of the "oxygenous" death.) Byull. *eksp. Biol. Med.*, 1942, *14*(2): 46–49.

1674. Rosenthal, J. Untersuchungen über den respiratorischen Stoffwechsel. *Arch. Anat. Physiol., Lpz.*, Physiol. Abt., 1902, (Suppl.) 278–293. [P]

VI. NOXIOUS AGENTS

A. GENERAL STUDIES OF NOXIOUS AGENTS

In common with other enclosed spaces, submarines, caissons, tunnel-faces, and diving helmets must be adequately ventilated to protect personnel from noxious agents. The practical aspects of these problems are considered in the section on ventilation (p. 244). Here, we shall be concerned with the effects of various deleterious substances upon the human body under conditions of acute and chronic exposure. Great strides have been made in the protection of personnel by attention to air conditioning and many of the problems to be discussed in relation, for example, to carbon monoxide, are no longer encountered in submarines or subaqueous construction operations. Nevertheless, reports dealing with these problems are included since they not only form an integral part of the history of the development of the subject but also they are of potential concern in new developments in submarine construction and operation or in underwater engineering. Safety of personnel is

insured only by constant attention to the details involved in providing pure air. There seems ample justification, therefore, for including the literature listed below. The reader will note that not only are papers specifically relating to noxious agents in submarines, diving, and subaqueous construction presented, but also representative reports dealing with the physiological and medical aspects of noxious substances in general are given. It is not asserted, for example, that all of the literature on carbon monoxide is included; however, an attempt has been made to bring together references which may be particularly useful to the medical officer or research worker concerned with submarine or compressed air medicine.

In 1911, Cohn (*1676*) published a short note on submarine cruising, outlining the symptoms of poisoning with carbon monoxide and gasoline fumes. Reference was also made to the injurious effects of high concentrations of carbon dioxide. Gasoline poisoning may be acute or subacute. In its acute manifestations there may be unconsciousness, slow, shallow breathing, feeble pulse, and pale, moist skin. The patient may have convulsions and intense frontal headache on return to consciousness. Repeated attacks lead to cardiac irritability, and may necessitate transfer from duty involving danger of exposure to gasoline fumes. Other hazards encountered by submarine personnel due to dampness, low temperatures, poor ventilation, and close, cramped quarters were referred to, and the author also discussed inadequate garbage disposal methods and toilet facilities in submarines. Conjunctivitis due to battery gases was also mentioned, and Cohn urged the installation of ventilating systems and closed toilet compartments. Since this report was written, great advances have been made in submarine construction and ventilation from the point of view of habitability.

A short statement on the effect of toxic gases in relation to occupational diseases was published by Holtzmann and Koelsch (*1681*) in 1914. The reader desiring a general source of reference to noxious agents may also refer to a volume on industrial health by Kober and Hayhurst (*1682*) published in 1924. DuBois' article (*1677*) which appeared in 1929 is also a valuable source of information on noxious gases and protective devices. Haldane's experiments on the deleterious effects of carbon monoxide at various blood saturation levels are discussed. Reference is made to the toxic action of hydrocyanic acid gas and various gases used in warfare. The history of the development of the gas mask is also described in some detail, and information is also given on apparatus for the administration of oxygen. The report contains a good bibliography.

The reader may refer to a long monograph by Flury and Zernik (*1678*) published in 1931 for an authoritative discussion of various types of toxic gases. Panse's report (*1683*), which appeared in 1931, may also be consulted, particularly for information on toxic substances such as arsene and carbon monoxide. This paper also contains a useful bibliographical list. Other sources of reference are papers or monographs by Bowditch, C. K. Drinker, P. Drinker, Haggard, and Hamilton (*1675*) 1940; Führer (*1679*) 1943; and Rossiter (*1684*) 1943. The second edition of Henderson and Haggard's monograph on noxious gases (*1680*) 1943 may be consulted as a standard work on the subject.

The reader should also make use of a report by Yant (*1685*) published in 1944. This report is a comprehensive review of gases, vapors, dusts, fumes, and mists having harmful effects upon the body.

1675. Bowditch, M., C. K. Drinker, P. Drinker, H. H. Haggard, and A. Hamilton. Code for safe concentrations of certain common toxic substances used in industry. *J. industr. Hgy.*, 1940, *22:* 251.

1676. Cohn, I. F. Notes on submarine cruising. *Nav. med. Bull., Wash.*, 1911, *5:* 455–457. [R]

1677. DuBois, E. F. Physiology of respiration in relationship to the problems of naval medicine. Part V. Noxious gases and protective devices. *Nav. med. Bull., Wash.*, 1929, *27:* 22–42. [R]

1678. Flury, Ferdinand, and Franz Zernik. *Schädliche Gase, Dämpfe, Nebel, Rauch- und Staubarten; mit autorisierter Benutzung des Werkes: Noxious Gases von Henderson und Haggard.* Berlin, Julius Springer, 1931, xii, 637 pp. [R]

1679. Führer, Hermann. *Medizinische Toxikologie. Ein Lehrbuch für Ärzte, Apotheker und Chemiker.* Leipzig, Georg Thieme, 1943, xii, 295 pp. [R]

1680. Henderson, Yandell, and Howard W. Haggard. *Noxious gases and the principles of respiration influencing their action.* Second and revised edition. New York, Reinhold Publishing Corporation, 1943, 294 pp. [R]

1681. Holtzmann, [ ] and [ ] Koelsch. Fortschritte in der Lehre von den Gewerbekrankheiten. *Dtsch. med. Wschr.*, 1914, *40:* 130–132. [R]

1682. Kober, George M. and Emery R. Hayhurst. *Industrial Health.* Philadelphia, P. Blakiston's Son & Co., 1924, lxxii, 1184 pp. [R]

1683. Panse, F. Beziehungen von Gewerbekrankheiten zum Nervensystem. *Zbl. ges. Neurol. Psychiat.*, 1931, *59:* 129–161; 273–302. [B, R]

1684. Rossiter, F. S. Some of the poisonous gases. Pp. 278–287 in: *The principles and practice of industrial medicine.* Edited by Fred J. Wampler. Baltimore, The Williams & Wilkins Company, 1943, xiv, 579 pp. [R]

1685. Yant, W. P. Gases, vapors, dusts, fumes and mists. Pp. 28–68 in: *Introduction to Industrial Medicine.* Edited by T. Lyle Hazlett. Pittsburgh, University of Pittsburgh, 1944, 216 pp. [R]

B. NOXIOUS GASES

1. CARBON MONOXIDE

(a) Carbon Monoxide in Submarines, Diving, and Tunnel Operations.

In 1938, Dorello (*1688*) reported 29 cases of poisoning among Italian submarine personnel in which there was abdominal pain, diarrhea, cough, and oppression in the chest, considered by the author to be due probably to carbon monoxide and various other products of combustion of fuel used in the Diesel engines. The report also discussed poisoning by arsenuretted hydrogen (arsene), methyl chloride, and various hydrocarbons liberated as the result of partial combustion of lubricating oils.

In 1936, Nimmo (*1696*) reported an accident to a diver in which carbon monoxide poisoning occurred as a result of exhaust gas from a leaky engine getting into the compression pump and contaminating the air delivered to the helmet. The diver in question worked on the bottom at 19 fathoms for 1½ hours and was then brought to 10 fathoms. After 10 minutes at this level, he was raised to 6 fathoms. He signaled for more air and then, as he did not answer, he was brought to the surface. He was unconscious and since it was believed that he was suffering from diver's paralysis, he was sent down again. Rescuers also had symptoms of headache and loss of control of the limbs and, in all, four men were affected; two of these died. It was found that guinea pigs placed in the helmet became drowsy after 15 minutes and then collapsed. Post-mortem examination of these animals revealed that the blood was a bright red color. To prevent further accidents of this type, the air intake was installed outside so that fresh air only was drawn into the compressor. Under these conditions, no further difficulties were experienced. There was no doubt but that the divers in question had been inhaling small quantities of carbon monoxide. These amounts of gas, which might not have been sufficient to cause death at normal pressure, became lethal as the pressure increased.

In 1942, Harris, Greenburg, and Werner (*1691*) discussed the hazards associated with Diesel engines used in tunneling. These engines liberate in the exhaust such substances as carbon monoxide, carbon dioxide, oxides of nitrogen and sulfur, aldehydes, and smoke. The Department of Labor, Division of Industrial Hygiene of New York State conducted extensive hygienic studies on Diesel engines under actual operating conditions in tunnels. These engines were used in operating trucks, bulldozers, and locomotives. It was concluded that Diesel-power machinery can be safely used underground if certain rules are obeyed. A 20 to 1 minimum air-fuel ratio was considered essential and the exhaust gases should be cooled and scrubbed before being liberated. The limit of carbon monoxide concentration was set at 0.002 percent and a minimum of 10,000 cu. ft. of air per minute of mechanical ventilation was to be maintained in any area for every engine operated within that area.

A short report on carbon monoxide in railway tunnels published in 1900 by Mosso, Benedicenti, Treves, and Herlitzka (*1694*) may also be consulted. Reference may be made, as well, to a paper on acute poisoning from carbon monoxide and petrol fumes on board submarine chasers, published by Charpentier (*1687*) in 1919.

In 1936, Bernz and Drinker (*1686*) called attention to a case of carbon monoxide poisoning in a sand blaster. The compressed air as supplied was free of carbon monoxide but apparently a broken exhaust valve heated and partially burned the lubricating oil. Medical examination in this case indicated that carbon monoxide was the cause of death.

That carbon monoxide poisoning may occur within an enclosed space in which there is inadequate ventilation is indicated in two reports by Irving, Scholander, and Edwards (*1692*) in 1942, and Scholander, Irving, and Edwards (*1697*) in 1943, who found that, in tents and snow houses, a primus stove may liberate appreciable quantities of carbon monoxide. However, the conditions leading to serious cases of poisoning which have been reported among Arctic explorers cannot yet be explained, according to the authors. Other papers on the toxic effects of exhaust gases have been published by the following authors: Jenkins (*1693*) 1932, Flury (*1690*) 1936, de Viveiros (*1698*) 1940, Eurich (*1689*) 1943, and Neighbors and Garrett (*1695*) 1931-32. The latter two reports contain case histories.

1686. Bernz, N. R. and P. Drinker. Carbon monoxide poisoning from compressed air. *J. industr. Hyg.*, 1936, *18:* 461. [Ch]

1687. Charpentier, [ ]. Intoxication par les gaz à bord des chasseurs de sous-marins. *Arch. Méd. Pharm. nav.*, 1919, *108:* 110–117. (Ch]

1688. Dorello, R. M. F. Su di un caso di intossicazione collettiva a bordo di un sommergibile. *Ann. Med. nav. colon.*, 1938, *44:* 213–222. [M]

1689. Eurich, F. W. Non-fatal effects of exhaust-fume poisoning. *Brit. med. J.*, 1943, *1:* 326. [Ch]

1690. Flury, F. Motorisierung und Vergiftungsgefahren. *Dtsch. Militärarzt*, 1936, *1:* 276–282.

1691. Harris, W. B., L. Greenburg, and G. Werner. Safeguards for use of Diesel engines in tunneling. *Industr. Hyg. Bull.*, 1942, *21*(11): 414–417. [M]

1692. Irving, L., P. F. Scholander, and G. A. Edwards. Experiments on carbon monoxide poisoning in tents and snow houses. *J. industr. Hyg.*, 1942, *24:* 213–217. [P]

1693. Jenkins, C. E. The haemoglobin concentration of workers connected with internal combustion engines. *J. Hyg., Camb.*, 1932, *32:* 406–408.

1694. Mosso, A., A. Benedicenti, Z. Treves, and A. Herlitzka. La respiration dans les tunnels et l'action de l'oxyde de carbone. Analyses et études faites sur la demande du Ministère des Travaux publics dans les tunnels *dei Giovi* (Chemins de fer Gênes-Novi) et dans l'Institut Physiologique de Turin. *Arch. ital. Biol.*, 1900, *34:* 357–361. [P]

1695. Neighbors, D. and C. C. Garrett. Carbon monoxide poisoning, with report of a case. *Tex. St. J. Med.*, 1931–32, *27:* 513–516. [Ch]

1696. Nimmo, J. R. Carbon monoxide poisoning whilst diving. *Med. J. Aust.*, 1936, *2:* 497–498. [Ch]

1697. Scholander, P. F., L. Irving, and G. A. Edwards. Factors producing carbon monoxide from camp stoves. *J. industr. Hyg.*, 1943, *25:* 132–136. [P]

1698. Viveiros, L. B. de. A intoxicação pelos gazes do motor. (Problemas médico-higiênicos de aviação). *Arch. brasil. Med.*, 1940, *30:* 221–235.

(b) General Studies on Carbon Monoxide

For an authoritative review of carbon monoxide poisoning in general, the reader is referred to a long article by Sayers and Davenport (*1711*) published in 1937. An excellent bibliography of 243 items is provided as well as sections on the history of the development of the subject, the occurrence of carbon monoxide poisoning, symptomatology, diagnosis, pathology, prevention, and treatment. Reference is made to work done by the U. S. Bureau of Mines on carbon monoxide for the New York State Bridge and Tunnel Commission in a report published in 1922 by Sayers (*1710*). This report also contains a useful review of the deleterious effects of high concentrations of carbon dioxide and of high temperatures and humidity.

Papers by Rossiter (*1707*, *1708*, *1709*) on carbon monoxide published in 1942, 1943, and 1944 should also be consulted. Rossiter (*1708*) stated that, at first, absorption of carbon monoxide is rapid and is then slowed down as the saturation of the blood with the gas increases. A greater amount of carbon monoxide is absorbed during the first hour than in succeeding hours. Inhalation of a given concentration of carbon monoxide in the air results in a certain definite maximum saturation of the blood. For instance, with a concentration of 0.01 percent, the maximum saturation of the blood is 17 percent, and with a carbon monoxide concentration in the air of 0.05 percent, the maximum saturation reached by the blood is 40 percent. Inhalation of high concentrations of carbon monoxide saturates the blood very rapidly, and death

may result after but a few inhalations. The rate of elimination is at first rapid and then slows down as saturation decreases, provided that the victim is breathing. Rossiter stated that, regardless of how high the percentage saturation of the blood has been, nearly all the gas is eliminated within 8 to 10 hours. A small amount of carbon monoxide may remain in the blood much longer. About one-half of the gas is eliminated in the first hour. Carbon monoxide does not remain within the body for periods of days, and once the gas is eliminated, it is found that the red blood corpuscles have not been destroyed or altered in any way and that they are capable of immediately resuming their normal function.

At blood saturation levels up to 20 percent, no symptoms are encountered. Between 20 and 30 percent saturation, there is flushing, a sense of tightness in the forehead, and slight headache. Between 30 and 40 percent, headache usually becomes severe, and there may be dimness of vision, weakness, dizziness, nausea, and sometimes vomiting; between 40 and 50 percent, the symptoms become more pronounced and pulse and respiratory rates are accelerated. At approximately 50 percent saturation or above, unconsciousness usually supervenes and between 60 and 70 percent, the heart action and respiration become depressed. At about 80 percent saturation, life is no longer possible. At first, subjects exposed to carbon monoxide may show evidences of muscular twitching, convulsions, tremors, loss of memory, mental confusion, hysteria, delirium, or paralysis. When high concentrations of the gas are inhaled, the victim may not show a train of symptoms but may suddenly collapse. In these cases, death follows paralysis of the respiratory center due to severe anoxemia.

Regarding prognosis, Rossiter points out that, if the victim is not found dead, nearly all patients recover within a few hours to several days. All the damage occurs while the carbon monoxide gas is combined with the blood, and it appears that the only harmful effect of carbon monoxide is the resulting anoxia of the tissues. In some cases, this anoxia may lead to destruction of brain cells with permanent after-effects such as loss of memory, paralysis, etc. These sequelae are comparatively rare but are more likely to be encountered in those of advanced years or in patients with arteriosclerosis. From personal observations over a period of 30 years, Rossiter concluded that chronic carbon monoxide poisoning does not exist. He stated that there is no anoxia unless severe gassing has taken place and the victim has been rendered unconscious. While it is true that men exposed over long periods to small quantities of the gas do attribute various complaints to carbon monoxide, nevertheless, Rossiter has arrived at the conclusion that all their symptoms are traceable to other underlying conditions.

Sievers, Edwards, Murray, and Schrenk (*1761*) 1942 made a study of 156 men of an average age of 41 who had been employees in the Holland Tunnel and who had been exposed to an average concentration of carbon monoxide of 0.7 parts per 10,000 daily for 13 years. No evidence of damage to the health attributable to carbon monoxide could be adduced. Shillito, Drinker, and Shaughnessy (*1781*) in 1936 reported an investigation of 21,143 cases of carbon monoxide poisoning in New York City, all requiring hospitalization, in which only 43 showed any after-effects. Of this number, 23 recovered, 11 died, and only 9 exhibited chronic after-effects. All of these were referable to the nervous system.

Regarding treatment, Rossiter emphasized the urgency of removal of the patient to fresh air, loosening the clothing at the neck, and institution of artificial respiration immediately if the victim is not breathing. Artificial respiration should be maintained for at least 2 hours or until normal breathing is resumed. When available, pure oxygen or a mixture of 93 percent oxygen and 7 percent carbon dioxide should be given in conjunction with artificial respiration. It is also advantageous to administer oxygen mixtures even in those cases where artificial respiration is unnecessary. In certain severe cases, Rossiter did not favor the use of carbon dioxide since it may unduly stimulate the over-taxed respiratory center. A resuscitator may be used if such an apparatus is at hand but it is essential that

rescuers do not wait for it to arrive but that they start artificial respiration at once. Warmth, massage, and maintenance of an airway are important adjuncts to treatment. Exertion should be guarded against, immediately after recovery. The use of methylene blue and venesection were condemned by Rossiter. However, intravenous injection of hypertonic saline solutions with glucose may be indicated for the relief of edema of the brain in the presence of symptoms of raised intracranial pressure. Rossiter's report contains a brief statement concerning various tests for carbon monoxide in air and in the blood.

Other general studies of carbon monoxide to which reference may be made are reports by Apfelbach and Hayhurst (*1699*) 1924; Maxwell (*1705*) 1933; Sayers and Davenport (*1711*) 1937; Drinker (*1701*) 1938; McNally (*1706*) 1939; Schulze and Beck (*1712*) 1939; Killick (*1704*) 1940; Beck, Roetman, and Suter (*1700*) 1942; Kammer and Carleton (*1703*) 1943; and the U. S. Department of Labor, Division of Labor Standards (*1713*) 1943.

Reference may be made to a review by Fulton and Hoff (*1702*) 1945 which contains a brief statement of the hazards of carbon monoxide in aircraft. Carbon monoxide in exhaust gases constitutes the principal noxious gas danger in aviation, and a vital objective of modern work in this field is the service application of techniques for detecting concentrations of carbon monoxide in aircraft under various conditions. There is need for an instrument which will produce a continuous record of fluctuations in the level of carbon monoxide in the airplane during flight. Warning devices which will set off an alarm at a given carbon monoxide concentration are being incorporated.

Certain research groups have been actively engaged in the problem of determining the combined effects of carbon monoxide and low oxygen tension upon physiological processes. As a preliminary criterion, an oxyhemoglobin saturation of 85 percent has been taken as a suitable minimum level. Any concentration of carbon monoxide, with or without low oxygen tension, which produces an effect equivalent to an oxyhemoglobin saturation of 85 percent might then be considered to be the maximum tolerable amount. The time required to reach a given carboxyhemoglobin concentration will depend to some extent upon the physical activity of the individual as well as upon the altitude to which he is exposed. Because of this time-concentration factor, it is difficult to establish a maximum air concentration of carbon monoxide for flight operations. These considerations are of importance in relation to submarine operations, particularly on long submerged patrols in which the oxygen percentage falls to low levels. With the likelihood that new technical developments in submarine construction will permit even longer periods of submergence than are now possible, the question of the effect of carbon monoxide in combination with low oxygen tensions assumes new significance.

1699. Apfelbach, G. L. and E. R. Hayhurst. Carbon monoxide poisoning. Pp. 369–411 in: *Industrial health.* Edited by George M. Kober and Emery R. Hayhurst. Philadelphia, P. Blakiston's Son & Co., 1924, lxxii, 1184 pp. [R]

1700. Beck, H. G., E. T. Roetman, and G. M. Suter. A report on the combustion products study. *W. Va. Univ. Bull.*, 1942, Ser. 43, No. 2–1: 1–60. [R]

1701. Drinker, Cecil K. *Carbon monoxide asphyxia.* New York, Oxford University Press, 1938, xx, 276 pp. [B, R]

1702. Fulton, J. F. and E. C. Hoff. Aviation medicine. Pp. 213–241 in: *The cylopedia of medicine surgery and specialties.* Edited by F. A. Davis Company. Philadelphia, 1945, 1080 pp. [B, R]

1703. Kammer, A. G. and E. H. Carleton. Carbon monoxide asphyxia. *Rocky Mtn. med. J.*, 1943, *40:* 234–240. [R]

1704. Killick, E. M. Carbon monoxide anoxemia. *Physiol. Rev.*, 1940, *20:* 313–344. [R]

1705. Maxwell, M. H. Carbon monoxide poisoning. *W. Va. med. J.*, 1933, *29:* 428–432. [R]

1706. McNally, W. D. Carbon monoxide poisoning. *J. Mich. med. Soc.*, 1939, *38:* 871–877. [R]

1707. Rossiter, F. S. Carbon monoxide. *Industr. Med.*, 1942, *11:* 586–589. [R]

1708. Rossiter, F. S. Carbon monoxide. Pp. 269–277 in: *The principles and practice of industrial medicine.* Edited by Fred J. Wampler. Baltimore, The Williams & Wilkins Company, 1943, xiv, 579 pp. [M, B, R]

1709. Rossiter, F. S. Carbon monoxide. Pp. 104–122 in: *Introduction to Industrial Medicine.* Edited by T. Lyle Hazlett. Pittsburgh, University of Pittsburgh, 1944, 216 pp. [M, R]

1710. Sayers, R. R. Prevention of illness among miners. *Rep. Invest. U. S. Bur. Min.*, 1922, no. 2319: 1–9. [R]

1711. Sayers, R. R. and S. J. Davenport. Review of carbon monoxide poisoning: 1936. *Publ. Hlth Bull., Wash.*, 1937, no. 195: 1–128. [R]

1712. Schulze, W. H. and H. G. Beck. Carbon monoxide—an industrial compensation problem. *Amer. J. med. Jurisprud.*, 1939, 2: 347–353.

1713. U. S. Department of labor. Division of labor standards. *Carbon monoxide poisoning. Cause and prevention.* Industrial health series no. 4. Washington, D. C., Govt. print. off., 1943, 5 pp. [R]

1714. Von Oettingen, W. F. Carbon monoxide: its hazards and the mechanism of its action. *Publ. Hlth. Bull., Wash.*, 1944, no. 290: 1–227. [M, B, R]

(c) Bodily Responses to Carbon Monoxide

In 1901, Mosso (*1735*) reported studies on the effects of various concentrations of carbon monoxide on human subjects in an enclosed chamber. One subject breathed air containing 0.02 percent carbon monoxide for 1 hour with no effects. Similarly, there were no symptoms in the same subject 2 days later with 0.03 percent carbon monoxide. Two days following, the subject breathed a mixture containing 0.04 percent carbon monoxide without harm and also tolerated a concentration of 0.08 percent carbon monoxide without distress. He was able to breathe 0.1 percent carbon monoxide for 15 minutes without feeling untoward effects, but there was a rise in respiratory rate and pulse. On remaining in the chamber for 1 hour and 40 minutes in an atmosphere in which the carbon monoxide concentration rose gradually to 0.3 percent (22 minutes being the time at maximum concentration), there were no ill effects. The same subject did not feel ill after 30 minutes in an atmosphere in which the carbon monoxide concentration rose to 0.33 percent (15 minutes at maximum). Breathing air containing 0.35 percent carbon monoxide, the subject began to experience malaise. He left the chamber after a run of 1 hour and 25 minutes (35 minutes at maximum concentration). There was a slight rise in pulse and fall in respiratory rate and also headache. On remaining for 55 minutes in a concentration of 0.37 percent carbon monoxide, there was pounding at the temples, vertigo, and nausea. The pulse rate rose from 83 to 112 and the respiratory rate fell from 26 to 24. Another subject remained for 50 minutes with a concentration at 0.4 percent. The pulse rose from 60 to 70 and there was vertigo and nausea. Mosso reported increased muscular fatigue, as measured by performance on the ergometer, after breathing carbon monoxide and tunnel gases.

Sayers, Meriwether, and Yant (*1738*), in their report in 1922 on the physiological effects of exposure to low concentrations of carbon monoxide, found that subjecting human subjects to 2 parts of carbon monoxide in 10,000 of air for 6 hours resulted in very mild symptoms of carbon monoxide poisoning at the end of the test. The saturation of the hemoglobin with carbon monoxide rose to 16 to 20 percent. There were no delayed effects after the test. Exposure of the subjects to 3 parts of carbon monoxide in 10,000 of air resulted in a saturation of 22 to 24 percent of the hemoglobin with carbon monoxide after 4 hours and 26 to 27 after 5 hours. At the end of 2 hours breathing this mixture, there were no symptoms; after 4 hours, mild effects were noted; after 5 hours, there were moderate symptoms. Exposure to 4 parts of carbon monoxide per 10,000 of air caused a saturation of 15 to 19 percent of the hemoglobin with carbon monoxide at the end of 1 hour, and 21 to 28 percent at the end of 2 hours. There were moderate after-effects. With subjects engaged in strenuous exercise, exposure for 1 hour to 2.5 parts of carbon monoxide per 10,000 of air resulted in moderate symptoms of carbon monoxide poisoning at the end of the test and a saturation of 14 to 16 percent of the hemoglobin with carbon monoxide. Under conditions of strenuous exercise, exposure for 1 hour to 3.3 parts of carbon monoxide in 10,000 of air caused a saturation of 17 percent of the hemoglobin and mild to moderate symptoms of carbon monoxide poisoning and mild after-effects. Exposure for 1 hour to 4 parts of carbon monoxide per 10,000 under conditions of exercise resulted in a saturation of 23 percent of the hemoglobin and again moderate symptoms of carbon monoxide poisoning. With the subject at rest and temperature and humidity raised, exposure for 1 hour to 3.1 parts of carbon

monoxide in 10,000 of air caused a saturation of 16 percent of hemoglobin and mild to moderate symptoms with moderate aftereffects. It was concluded that the rate of combination of carbon monoxide with hemoglobin is slow with low concentrations of carbon monoxide and under conditions of rest and that the combination of carbon monoxide with hemoglobin is more rapid during the first hour than during any succeeding hour with the subject at rest. Exercise resulted in an acceleration of the combination of carbon monoxide with hemoglobin, and the symptoms tended to be emphasized by exercise. Under conditions of high temperature and humidity, the combination of carbon monoxide with hemoglobin was more rapid than with normal temperature and humidity. All symptoms studied were acute and no permanent deleterious effects from exposure to carbon monoxide were demonstrable.

The general pathological changes in fatal carbon monoxide poisoning have been reviewed by Martland (*1728*) 1934. He pointed out that patients may die suddenly and quickly; they may recover completely; or they may remain comatose for 1 to 3 days and then die. In a few cases, the patients may be left with permanent psychoses.

The action of carbon monoxide on the body depends upon its interference with the oxygen transport mechanism in the blood. Haldane (*1726*) 1895 showed that the proportion of oxyhemoglobin formed depended not only upon the concentration of carbon monoxide inhaled but also upon the oxygen tension. With pure oxygen replacing air, a higher percentage of carbon monoxide was needed to produce symptoms in mice than when air mixtures were breathed. Dilution of the air with nitrogen or hydrogen decreased the amount of carbon monoxide necessary to cause symptoms of poisoning or death.

Benedicenti and Treves (*1718*) 1900 found that the effects of carbon monoxide upon dogs were comparable to the changes produced by gradual rarefaction of the air or reduction of the oxygen percentage, but it was considered that carbon monoxide in large doses might have a direct paralyzing action upon the heart. In 1901, Mosso (*1732*) compared carbon monoxide poisoning with mountain sickness, and considered that carbon monoxide acted solely through its anoxic effect. In both conditions, there were acceleration of the heart (ascribed to vagal paralysis), muscular weakness, slow and shallow respiration, and periodic breathing. Mosso (*1733*) 1901 observed that animals succumbing to carbon monoxide showed edema of the lungs with hyperemia and ecchymosis especially at the border of the lobes and pointed out that human subjects poisoned by carbon monoxide may die of pneumonia within a few days. These pathological effects upon the lungs were considered to be due to the paralyzing effect of carbon monoxide upon the vagus nerve. Campbell (*1720*, *1721*) 1929 and 1929–30 also stated that the effects produced by carbon monoxide are similar to those associated with breathing an atmosphere containing a low oxygen tension. The relation between oxygen lack and carbon monoxide poisoning was also discussed by LeMessurier (*1727*) in 1943.

For information on the rate of carbon monoxide uptake in man, reference may be made to Roughton (*1737*) 1945 and Forbes, Sargent, and Roughton (*1725*) in 1945. In the first of these reports, the time which the blood spends in passing through the lung capillaries is considered in relation to the rates of carbon monoxide uptake and elimination.

In 1901, Mosso (*1731*) subjected rabbits to atmospheres of pure carbon monoxide and found an immediate fall in blood pressure and slowing of the heart. Upon withdrawal of carbon monoxide, after about 10 seconds, there was a rise in blood pressure above normal, with increased force of contractions. A similar but more profound reaction was observed on administration of carbon monoxide for 24 seconds. These and other experiments on animals lead Mosso to the conclusion that carbon monoxide produces a central vagal paralysis. In addition, in the case of large doses of carbon monoxide there was also considered to be a local inhibiting action on the heart muscle itself. The central effects of carbon monoxide were seen to provide a mechanism for over-

coming undue slowing of the heart as a result of the peripheral effect.

Campbell (*1722*) in 1932–33 reported hypertrophy of the heart in mice gradually acclimatized to an atmosphere containing 0.24 percent carbon monoxide and kept under such conditions for 225 days. The question was raised as to whether this increase in the size and weight of the heart was associated with increased blood viscosity. Campbell found that under such conditions of chronic carbon monoxide exposure, the development of neoplastic conditions in mice was retarded. Cardiac deviations in carbon monoxide poisoning were discussed by Schweitzer and Bosch (*1739*) in 1942.

Regarding the action of carbon monoxide on the blood, Von Oettingen (*1741*) in 1939 stated that not only does carbon monoxide combine with hemoglobin, but also the presence of carboxyhemoglobin inhibits the dissociation of oxyhemoglobin so that less oxygen is released to the tissues. It was also considered possible that carbon monoxide might unite with myoglobulin. It was held that in carbon monoxide poisoning there is a greater tendency to heart failure than is the case in other anoxemias.

In severe carbon monoxide poisoning, Chiodi, Dill, Consolazio, and Horvath (*1723*) 1941 found that the respiratory center was depressed. The cardiac output showed only slight increases with carboxyhemoglobin saturations ranging up to 30 percent. From that level up to the 50 percent carboxyhemoglobin, the cardiac output increased by as much as one-half. The authors stated that severe carbon monoxide poisoning incompatible with life has a direct depressant action on the respiratory center. Regarding the affinity of hemoglobin for carbon monoxide, Foà (*1724*) in 1900 stated that intracellular hemoglobin combined more quickly with carbon monoxide than does the hemoglobin in the plasma. Nasmith and Graham (*1736*) 1906–7 reported that guinea pigs can live almost indefinitely in a carbon monoxide-air atmosphere of such a concentration as to give a 35 percent saturation of the blood with carbon monoxide. They found leucocytosis with a relative eosinophilia and an increase in the red blood cell count and the quantity of hemoglobin. Erythroblasts appeared in the blood and then disappeared. Brieger (*1719*) 1944 found that in acute carbon monoxide poisoning, polycythemia occurred, but not invariably. Sometimes, there was actually a decrease in the red blood count and the amount of hemoglobin. Permanent polycythemia was seen in one dog. Six dogs were subjected for 11 weeks to an atmosphere containing 0.0096 percent of carbon monoxide, leading to a blood saturation of 20.1 percent carboxyhemoglobin. At the end of 9 weeks, there was a significant increase in the red blood count, and the hemoglobin showed a definite increase. These values decreased, during continued exposure, to and slightly below the original level. Polycythemia did not prevent the noxious effects of carbon monoxide upon the circulation or the nervous system in acute or chronic poisoning.

Williams and Smith (*1744*) 1934-35 reported experiments in which they exposed white rats to illuminating gas for 1 hour a day for many days; the gas mixture contained 0.34 percent carbon monoxide. After 200 days, there was a slight increase in blood cell fragility and an increase in the red blood cell count. The hemoglobin values were 2 to 5 percent higher in gassed animals than in controls. The general condition of the animals subjected to carbon monoxide was poor; the coats were shabby; and there was decreased appetite and a fall in body weight as well as loss in muscle tone. There was no increased predisposition to infection. After 14 days' exposure to the experimental conditions, the animals did not mate.

According to Miura (*1730*) 1936–37, animals subjected to concentrations of 0.5 to 1.0 percent carbon monoxide showed first a fall in the serum albumin. As the carbon monoxide poisoning approached fatal levels, the serum albumin concentration and the colloidal osmotic pressure of the blood plasma increased beyond the original value. Likewise, the albumin-globulin ratio first decreased and then showed an increase. The nonprotein nitrogen values first decreased and then rose very gradually.

Regarding the effects of carbon monoxide inhalation upon metabolism, Walters (*1742*) 1927 found that exposure of animals to concentrations of 0.02 to 0.05 percent for 1 to 2 hours had no effect upon the metabolic rate but that, in some cases, there was a depression after 4 to 6 hours. At concentrations of carbon monoxide above 0.05 percent, there was almost always a depression in matabolic rate even after short exposure. It was found that the fall in metabolic rate was accompanied by a decrease in body temperature, and general symptoms of carbon monoxide poisoning were seen to parallel the slowing of metabolism. Mosso (*1734*) 1900 found that, in dogs, breathing a concentration of 0.25 percent carbon monoxide for 10 minutes resulted in a rise of temperature. Inhalation of carbon monoxide mixtures above 0.4 percent caused a fall in temperature. According to Benedicenti and Sandri (*1717*) 1900, there is a diminution and then an increase in reducing power of frog muscle in carbon monoxide poisoning; Audenino (*1715*) 1900 reported that carbon monoxide at first increased and subsequently lowered the excitability of the frog's gastrocnemius muscle. According to Wehmeyer (*1743*) 1900, muscles of the crayfish showed slower contractions and were more rapidly fatigued. Mosso (*1732*) 1901 found greater fatigability of muscular contraction in personnel exposed to carbon monoxide in tunnels.

In a certain number of cases, skin lesions have been observed in carbon monoxide poisoning. In 1911, McLean (*1729*) reported the case of a young man of 22 who had been found unconscious in a room in which a gas heater had blown out. He was sent to the hospital as soon as he was discovered. The temperature was 102° F., the leucocyte count was normal, as was the red blood cell count, but there was a tendency to clumping of the erythrocytes. For the first 48 hours, he was given oxygen inhalations and on the fourth day, the temperature was normal and he could sit up. On the fifth day, he walked around and was discharged. Seven days after exposure, he was readmitted to the hospital with pains in the legs and feet which were swollen and discolored. The discolored portions were cold and as time went on, these areas became gangrenous. Cultures taken 11 days later showed the organisms to be *Staphylococcus aureus*. The temperature fluctuated between 101° and 105° F.; the pulse varied between 130 and 160, and there was a marked leucocytosis with 85 percent polymorphonuclear leucocytes. On the twentieth day after exposure, one leg was amputated and the twenty-fourth day, the other leg. There were bed sores and much sloughing of tissue. A month later, he began to improve and 4 months after the original accident, he was discharged. A search for thrombosis and embolism revealed no such cause of disturbance of the peripheral circulation.

Wilson and Carey (*1745*) in 1940 also reported a case of gangrene of the foot following carbon monoxide poisoning. The victim was a man of 72 years of age who was overcome by illuminating gas. There was stupor and cyanosis, a rapid pulse and a temperature of 102° F. Six days after the accident, an area of ecchymosis appeared above the right mastoid and on the twenty-ninth day, the patient complained of burning sensation in the right foot which became progressively worse. During the second month, the foot was cold, cyanotic, and very painful. After 3 months, gangrenous areas developed between the toes of the right foot. The foot was amputated, and the patient succumbed 3 days later.

Seifert (*1740*) in 1943 reported the case of a man of 27 who was admitted to the hospital after having been found in a parked car with the motor running and the windows closed. He was in profound coma; the lips were cherry red and the face cyanotic; respiration was shallow and rapid. The pulse was accelerated, the blood pressure was 124/78, and the temperature 104.8° F. He was treated as for shock and 50 cc. of methylene blue solution and 250 cc. of citrated blood were injected intravenously. He was given intranasal oxygen, and later, another 250 cc. of whole blood. In 7 hours, he recovered consciousness. Forty-eight hours after admission, bright, cherry-red areas developed on the buttocks, heels, and scalp, as well as small blebs on the fingers of both hands. These disappeared, but the red-

dened erythematous area on the scalp and heels persisted. After 72 hours, these areas became softened; after 6 days, the soft areas of the scalp were covered with a scab and soon loss of hair over the area was noticed. Finally, the tissue became necrotic and gangrenous and on the tenth day began to slough. The gangrenous lesions of the heels each covered an area of about 4 square inches and sloughed out to a depth of about one-fourth inch. The scalp lesion healed in about 3 months, and the lesions on the heels healed by granulation in about 6 months.

Regarding effects of carbon monoxide upon visual function, the reader may refer to a brief statement by Benedicenti and Ricchi (*1716*) 1900 stating that railway personnel exposed to tunnel gases did not show changes in visual function until symptoms of general malaise and cardiac and respiratory disfunction supervened.

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(d) Chronic Carbon Monoxide Poisoning

As has been said, Rossiter (*1708*) came to the conclusion that chronic carbon monoxide poisoning did not exist. However, Beck (*1747*) 1926–27 referred to harmful effects of chronic exposure to carbon monoxide and stated that chronic cases may simulate such conditions as anemia, hyperthyroidism or so-called neurasthenic states. Herndon (*1755*) 1927 stated that most of the men alleging disability from exposure to bad air in mines are sick from diseases unrelated to the conditions of employment. Stagnant air was the most common cause of complaint among workers and carbon monoxide poisoning was the next most common cause of disability. Herndon concluded that exposures which do not cause loss of consciousness are practically never dangerous and there are no sequelae from such exposures. All so-called "late symptoms" were ascribed by Herndon to extraneous disease. Cases in which exposure is continued to the point of syncope and collapse almost invariably recover entirely or are fatal. Most late sequelae described in the literature were believed to be limited to those cases in which the patient had lived after a prolonged period of unconsciousness. Permanent illness due to carbon monoxide poisoning is relatively uncommon. The condition is one of simple suffocation, and when recovery takes place, it is rapid and complete.

It appears that mice can be acclimatized to 0.3 percent carbon monoxide in air by gradually increasing the concentration in the inspired air. Such mice usually gain more weight than controls but are not fertile, according to Campbell (*1753, 1754*) 1929–30 and 1933. Killick (*1758*) in 1937–38 reported that mice may be acclimatized to a concentration of carbon monoxide up to 0.25 percent by gradually increasing the gas concentration from a level of 0.03 percent. Increase in the red blood cell count, the reticulocyte count, and the blood volume, and enlargement of the spleen were observed. The effects of repeated exposure to carbon monoxide were also discussed by Killick (*1756*) in 1933.

In 1936, Killick (*1757*) attempted to acclimatize human subjects to carbon monoxide by repeated exposures to carbon-monoxide-containing atmospheres. Weekly exposures were given, each lasting 2 to 6 hours, and concentrations of carbon monoxide varying from 0.011 to 0.046 percent were used. The experiments were continued about 4 months. There was evidence of acclimatization lasting 13 to 18 months. Acclimatization was shown by a decrease in symptoms and also by the fact that longer exposures were needed to produce a given carboxyhemoglobin concentration for a particular air concentration of carbon monoxide. No change in the red blood count or hemoglobin count was observed on acclimatization. The symptoms during acclimatization were found to vary with the carboxyhemoglobin concentration of the blood. At blood concentrations below 30 percent, no symptoms were observed on exposure, although sometimes headaches occurred afterwards. At concentrations between 30 and 35 percent, there was throbbing in the head, headache, and nausea both during and after exposure. Between 35 and 42 percent, the subjects complained of headache, drowsiness, nausea, and vomiting with very severe post-exposure headache and vomiting. The question of the possibility of chronic carbon monoxide poisoning was also discussed by Martin (*1759*) 1938.

Beck (*1748*) 1936 stated that secondary symptoms associated with the central nervous system may develop several days after apparently successful recovery from acute carbon

monoxide anoxemia. Chronic anoxemia may be manifest, according to Beck, in such symptoms as depression, restlessness, fears, confusion, headaches, vertigo, and vasomotor instability. Other symptoms were stated to be dull ache or spasmodic pains localized in the back, shoulders, abdomen or chest, cardiospasm, generalized digestive disturbances, dysphagia, dyspnea, palpitation, lowered basal metabolic rate, nocturia, and dysuria. A further report on chronic carbon monoxide anoxemia was published by Beck (*1749*) in 1937, and in 1938 Beck and Suter (*1752*) described cases of myocardial disease allegedly due to chronic exposure to carbon monoxide. It was stated that carbon monoxide poisoning affects primarily the vascular system and that there is dilatation of the peripheral vessels, hemorrhage in vessel walls, edema, perivascular infiltration, epistaxis, and hemoptysis. The heart and the papillary muscles of the mitral valves and the walls of the left ventricle were stated to be particularly sensitive. Thrombi were believed to occur within small vessels and Beck and Suter stated that there may be rupture of the heart in acute poisoning by coal gas. Out of 136 cases attributed to carbon monoxide poisoning, the authors gave 5 case histories, the first being a typical case of parkinsonism. In the other cases, there were symptoms of angina pectoris. All cases with angina except one completely recovered symptomatically when the source of carbon monoxide was removed.

In 1939, Beck (*1750*) reported statistics to show that workers in gas plants exposed to carbon monoxide have twice as high an illness rate and lose 20 percent more time from work than personnel in any other occupation. Case histories were given of seven patients with symptoms similar to those of gastric ulcers. In six of these, recovery followed elimination of the source of carbon monoxide. The seventh patient died. Ulcers were not demonstrable in any of the patients.

Further evidence bearing upon the existence or nonexistence of chronic carbon monoxide poisoning is provided by reports by Sievers (*1760*) 1942 and Sievers, Edwards, Murray, and Schrenk (*1761*) 1942 on the effect of exposure to known concentrations of carbon monoxide on traffic officers stationed in the Holland tunnel for 13 years. The report included observations on 156 men, half of whom were on regular duty. The carbon monoxide in the tunnel air rose as high as 3 parts per 10,000 of air. Some subjects reported throbbing headaches, dizziness, anoxia, and nausea after a particular busy, hot, windless summer day. Only 3 men showed cardiac enlargement or electrocardiographic irregularities. Hypertension was found in 5 men and 17.5 percent exhibited tremors of the hand on examination. Marksmanship scores were not different from those of any comparable group studied. The erythrocyte counts were normal. Carboxyhemoglobin values were in proportion to the amount of smoking among the men. The authors concluded that the subjects showed no ill effects from carbon monoxide in the tunnel.

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(e) Nervous and Mental Disturbances Caused by Carbon Monoxide

Forbes, Cobb, and Fremont-Smith (*1764*) in 1924 demonstrated a rise of intracranial pressure and edema of the brain in carbon monoxide asphyxia in cats. Intravenous administration of hypertonic saline solution reduced the brain bulk and also relieved stupor and headache in clinical patients. A case of paralysis of the right leg and foot was reported by Kurlander (*1771*) in 1924, and Mackay (*1772*) in 1930 described a case in which a typical picture of parkinsonism appeared 2 months after asphyxiation. This patient was discovered in coma 18 hours after closing the doors of a garage. In 5 days, he was conscious but confused; speech was drawling and slow. On discharge at the end of 2 months, motor power and sensation were normal but movements were slow and irregular. Eight months after exposure the gait was still spastic.

As Shillito, Drinker, and Shaughnessy (*1781*) 1936 have pointed out, nervous and mental sequelae in carbon monoxide poisoning are relatively infrequent. Out of 21,143 cases of carbon monoxide poisoning in New York City, only 43 had any after-effects, and of these, only 9 showed chronic signs and symptoms referable to the nervous system. Although relatively infrequent, the mental and neurological sequelae of carbon monoxide asphyxia are often very trying from the point of view of treatment and are characterized by severe disability or deterioration of the personality. Raskin and Mullaney (*1777*) in 1940 reported the case of a woman victim of accidental carbon monoxide poisoning who survived for 15 years after the original accident and exhibited gross disturbances of neurological and mental function. She developed partial amnesia; there was diminished self-control, violent flare-ups of temper and she became secretive and subject to irrational behavior. As time went on, she became sleepless and restless, and developed tremors (chattering of the teeth). There were parasthesias, which she described as a "creepy feeling all over." There was also numbness of the legs. It became more and more difficult for her to concentrate and she was confused and tended to repeat words and phrases. She exhibited rhythmic picking at her clothes, tremors of the left arm and leg, exaggerated reflexes, bilateral ankle clonus, and a thick mumbling speech. There was poverty of ideas, and she had a rigid, inexpressive face with staring eyes. At autopsy, large bilateral, symmetric, necrotic lesions of the globus pallidus were seen and there were areas of softening and small glial scars throughout the cortex, with corresponding areas of demyelinization, mild vascular changes, and neuronal destruction in the caudate nucleus and Ammon's horn. In these areas, the tissue around many vessels was rarefied, took on a lighter stain and was wider meshed than the rest of the tissue. These typical pallidal lesions and the numerous small necrotic lesions in the cortex—some healed and some unrepaired—account for the clinical picture presented by this patient during the 15 years she lived after the accident.

A remarkable case with a favorable outcome was reported by Neilson (*1775*) in 1943. The report concerns a patient of 59 who was asphyxiated by exhaust gas and who went steadily downward for 2 years to a state of well-advanced parkinsonism. He showed characteristic immobile facies, tremor, and cogwheel rigidity. He became subject to generalized convulsions and there was deterioration of the personality. Three years after the accident, improvement began to set in and at 3 years and 8 months he was almost completely recovered and able to return to work.

The convulsions ceased and there were only a few remaining signs of injury.

Nichols and Keller (*1774*) in 1936–37 reported one case of a man who was revived after a suicidal attempt in which there was subsequent loss of ability to perform certain skilled acts. Agraphia was also present. Convulsive disorders subsequently developed due to severe visuomotor incoordination. The patient was unable to learn through concrete examples and a carefully planned retraining program was devised in which all instructions were completely verbalized. By this means, the function of written speech was returned to the patient.

A psychotic reaction in carbon monoxide poisoning was described by Menninger (*1773*) in 1936–37. The case reported was that of a 35-year-old lawyer who was found unconscious in a car in a garage. His subsequent course was characterized by a psychosis in which there were symptoms of depression and amnesia. There was also peripheral neuritis. When last seen, 13 months after the carbon monoxide poisoning, there was general improvement. It is to be noted that the poisoning may have been a suicidal attempt and that the patient was depressed and agitated even before the accident.

In a severe case of carbon monoxide poisoning reported by Sanger and Gilliland (*1779*) in 1940, coma lasted for 12 days. At the end of 16 days, the patient could speak but was uncooperative and surly. He did not recognize his friends and there was loss of memory. There were some signs of parkinsonism, namely, pill-rolling movements and a mask-like facies. These symptoms disappeared in about a month. He complained of severe pains in the legs and feet and there was toe drop on the right side. The peripheral neuritis, as well as other symptoms, disappeared slowly and in 1 year, he was able to resume his professional activities. In 2 years, he was completely well.

In 1942, Jensen (*1770*) reported the case of a man of 34 who attempted suicide by carbon monoxide. He was unconscious for 72 hours and was hospitalized for 2 weeks. Previously, he had been an excellent student, a skilled pianist, and a business executive. Eighteen months after poisoning, he exhibited schizoid disturbances. Space perception was impaired, and typing, playing the piano, and matching colors were impossible. There were no hallucinations or delusions. Slight improvement was noticed 10 months after the appearance of these symptoms.

The prognosis of carbon monoxide poisoning in 15 patients previously mentally ill was discussed in 1942 by Van Amberg (*1783*). Four of these who had had enough gas for acute symptoms, but were not unconscious, developed no neurological or mental changes. Four of the patients who were unconscious up to 30 minutes developed no new clinical signs or symptoms. In 2 patients who were unconscious for about an hour, transient neurological changes were seen. In 5 patients who were unconscious for 3 hours to 10 days, there was great variability of recovery. A patient poisoned with carbon monoxide is not likely to have serious sequelae, according to Van Amberg, if he regains consciousness within 1 hour after removal from the toxic atmosphere. Beyond this point, there appears to be no correlation between the duration of unconsciousness and the severity and permanence of the pathological and clinical changes. No important clinical difference was noted between the toxicity of motor exhaust gas and that of illuminating gas.

Three case histories showing neuritis following carbon monoxide poisoning were reported in 1924 by Wilson and Winkleman (*1784*). In the first case, the victim was unconscious on admission to hospital but a few days later could answer questions though disoriented. One week after exposure, the right hand and forearm became cold and pale, the patient lost consciousness and died 10 days after exposure. Sections of the peripheral nerves revealed swelling of the medullary sheaths. The right axillary artery was thrombosed. The second patient was found unconscious in a room heated by a charcoal burner. He survived for 11 days and finally succumbed to bronchopneumonia. On histological examination, there was degeneration and swelling of the peripheral nerves. The third patient was overcome by illuminating gas, treated at the

hospital, and discharged the same day. A few days later, he vomited. Seven days after exposure, he complained of pains in the feet and legs and developed coarse tremors of the extremities as well as tenderness on pressure over the nerve trunks and the brachial plexus. The lungs were emphysematous and the X-ray disclosed cardiospasm. He grew steadily worse and died of bronchopneumonia. No autopsy was performed but there were clinical signs of polyneuritis.

In 1882, Poelchen (*1776*) described cases illustrating carbon monoxide poisoning with softening of the brain. Destructive lesions were found in the corpus striatum. Hill and Semerak (*1767*) in 1918 also reported changes in the brain in carbon monoxide poisoning.

In 1920–21, Stewart (*1782*) reported histological findings in a patient who died of carbon monoxide poisoning. There was no gross pathology but the pia-arachnoid showed congested blood vessels. Zones of softening as well as proliferation of neuroglial cells were found in every area of the cortex. The Virchow-Robin spaces were filled with small round cells and there was wide-spread degeneration of the myelin sheaths of nerve fibers. Nerve cells in the pons and the medulla oblongata were swollen and degenerated. In the spinal cord, there was chromatolysis of the ganglion cells, and the left anterior horn was shrunken. The axis cylinders were abnormal and swollen and there was neuroglial proliferation.

Ruge (*1778*) in 1922 pointed out that softening of the nervous tissue as well as vascular changes in the middle portion of the lenticular nucleus are typical of carbon monoxide poisoning. Fatty changes occurred in the ganglion cells within 24 hours and there were small hemorrhages from blood vessels into the perivascular spaces. After 2 days, the changes in the lenticular nuclei were seen; on the fourth or fifth day, sharply demarcated foci of softening were observable. Within the foci of softening and in the surrounding area, there were hyperemia and severe changes in the nervous elements. The author considered that the changes in the nervous structures are primary and that later arteriosclerotic changes in blood vessels lead to further damage to ganglion cells.

In dogs killed by exposure to 0.6 percent carbon monoxide for 20 to 30 minutes (Chornyak and Sayers (*1763*) 1931), the brain as a whole showed severe perivascular and perineuronal edema. This was most marked in the corpus striatum, the cortex and the dorsal motor nuclei of the vagus nerves. There were petechial hemorrhages, especially in the corpus striatum and in the cortex. The neurones were extensively damaged and in some areas the cells were ruptured. In others, the cells showed chromatolysis and distorted nuclei, especially in the pons. Some cells, particularly the small pyramidal neurones of the cortex and cells of the dorsal nuclei of the vagus nerves, were shrunken and pyknotic. The dorsal motor nuclei of the vagus, the dorsal sensory areas of the brain stem, the corpus striatum, and the cortex were the areas mainly affected. There were individual variations in the degree of change in different dogs.

Chornyak and Sayers (*1763*) 1931 concluded that carbon monoxide poisoning resulted in vascular dilatation, stasis, and perivascular and perineuronal edema. Two types of degenerative change in the neurones were distinguished: (*a*) shrinkage of the cells with diffuse staining, and (*b*) varying degrees of chromatolysis. Essentially similar findings were reported by the same authors (*1780*) in 1936–37.

Herlitzka (*1766*) 1900 believed that carbon monoxide acted upon the central nervous system only by anoxemia and that it had no specific toxic effect. Further studies on the cause of central nervous system lesions in carbon monoxide poisoning were reported by Hiller (*1768*) in 1924 and Janz (*1769*) in 1942.

The question may be raised as to whether carbon monoxide in pure form gives rise to symptoms and signs similar to those encountered in illuminating gas or exhaust gas. The answer to this question is of considerable academic interest, but for practical purposes, carbon monoxide poisoning from the pure gas is not likely to be encountered.

1763. Chornyak, J. and R. R. Sayers. Studies in asphyxia. I. Neuropathology resulting from comparatively rapid carbon-monoxide asphyxia. *Publ. Hlth Rep., Wash.*, 1931, *46*(26): 1523–1530. [P]

1764. Forbes, H. S., S. Cobb, and F. Fremont-Smith. Cerebral edema and headache following carbon monoxid asphyxia. *Arch. Neurol. Psychiat., Chicago*, 1924, *11:* 264–281. [P]

1765. Gillies, H. Mental sequelae in acute carbon monoxide poisoning and brain injury. *J. R. nav. med. Serv.*, 1945, *31:* 60–62. [Ch]

1766. Herlitzka, A. Action de l'oxyde de carbone sur le système nerveux. *Arch. ital. Biol.*, 1900, *34:* 416–428.

1767. Hill, E. and C. B. Semerak. Changes in the brain in gas (carbon monoxid) poisoning. *J. Amer. med. Ass.*, 1918, *71:* 644–648. [P]

1768. Hiller, F. Über die krankhaften Veränderungen im Zentralnervensystem nach Kohlenoxydvergiftung. *Z. ges. Neurol. Psychiat.*, 1924, *93:* 594–646.

1769*. Janz, H. W. Über den Aufbau und die Enstehungsbedingungen cerebraler Krankheitsbilder nach Kohlenoxydvergiftung. (Zugleich Beitrag zur Kenntnis der zentralnervosen Reaktion auf hypoxämische Einwirkungen.) *Arch. Psychiat. Nervenkr.*, 1942, *114:* 539–593.

1770. Jansen, M. B. Mental deterioration following carbon monoxide poisoning. *Psychol. Bull.*, 1942, *39:* 586. [Ch]

1771. Kurlander, J. J. Paralysis of the leg following illuminating gas poisoning. *J. Amer. med. Ass.*, 1924, *83:* 271. [Ch]

1772. Mackay, R. P. Neurologic changes following carbon monoxide poisoning. *J. Amer. med. Ass.*, 1930, *94:* 1733–1736. [Ch]

1773. Menninger, W. C. Psychotic reaction in carbon monoxide poisoning. *Bull. Menninger Clin.*, 1936–37, *1:* 29–32. [Ch]

1774. Nichols, I. C. and M. Keller. Apraxias and other neurological sequelae of carbon monoxid asphyxia. With report of a case. *Amer. J. Psychiat.*, 1936–37, *93:* 1063–1072. [Ch]

1775. Nielson, J. M. Carbon monoxide parkinsonism with recovery after three years. *Bull. Los Angeles neurol. Soc.*, 1943, *8:* 22–24. [Ch]

1776. Poelchen, [ ]. Gehirnerweichung nach Vergiftung mit Kohlendunst. *Berl. klin. Wschr.*, 1882, *19:* 396–399. [C, Ch]

1777. Raskin, N. and O. C. Mullaney. The mental and neurological sequelae of carbon monoxide asphyxia in a case observed for fifteen years. *J. nerv. ment. Dis.*, 1940, *92:* 640–659. [Ch]

1778. Ruge, H. Kasuistischer Beitrag zur pathologischen Anatomie der symmetrischen Linsenkernerweichung bei CO-Vergiftung. *Arch. Psychiat. Nervenkr.*, 1922, *64:* 150–205. [B, Ch]

1779. Sanger, E. B. and W. L. Gilliland. Severe carbon monoxide poisoning with prolonged coma followed by transitory psychosis, peripheral polyneuritis and recovery. *J. Amer. med. Ass.*, 1940, *114:* 324. [Ch]

1780. Sayers, R. R. and J. Chornyak. Neuropathology attending asphyxia from carbon monoxide and atmospheres deficient in oxygen. *Arch. Gewerbepath. Gewerbehyg.*, 1936–37, *7:* 1–7 [P]

1781. Shillito, F. H., C. K. Drinker, and T. J. Shaughnessy. The problem of nervous and mental sequelae in carbon monoxide poisoning. *J. Amer. med. Ass.*, 1936, *106:* 669–674. [R]

1782. Stewart, R. M. A contribution to the histopathology of carbon monoxide poisoning. *J. Neurol. Psychopath.*, 1920–21, *1:* 105–116 [Ch]

1783. Van Amberg, R. J. Prognosis of carbon monoxide poisoning in 15 patients, previously mentally ill. *Psychiat. Quart.*, 1942, *16:* 668–680. [Ch]

1784. Wilson, G. and N. W. Winkleman. Multiple neuritis following carbon monoxide poisoning. *J. Amer. med. Ass.*, 1924, *82:* 1407–1410. [Ch]

(f) Prevention and Treatment of Carbon Monoxide Poisoning

The essential features in prevention and treatment of carbon monoxide poisoning have been given by Rossiter in 1943 (*1708*) and by others. Here a number of papers dealing with special detailed points may be referred to. In 1901, Mosso (*1791*) found that a dog poisoned with 1 percent carbon monoxide, and apparently dead, recovered on being placed in a chamber filled with oxygen and compressed to 4 atmospheres of pure oxygen. Sayers and O'Brien (*1792*) 1922 and Sayers and Yant (*1793*) 1925 reviewed essential points of treatment. Henderson and Haggard (*1790*) 1922 recommended oxygen and carbon dioxide inhalation for carbon monoxide asphyxia as a method of rapid elimination of the carbon monoxide from the blood. They stated that in cases of carbon monoxide poisoning, artificial respiration should be started as soon as possible. When spontaneous breathing has been resumed, inhalation of oxygen containing 5 percent carbon dioxide maintains respiration and assists in washing out carbon monoxide from the blood. Carbon monoxide is stated to be eliminated about three times as rapidly with an oxygen-carbon dioxide mixture as with air alone. Treatment of carbon monoxide poisoning is also discussed by Henderson (*1788*, *1789*) 1930 and 1931–32 and by Haggard and Henderson (*1787*) 1921.

In 1929, Drinker and Shaughnessy (*1786*) advised increasing the concentration of carbon

dioxide to 7 percent (from 5 percent) and then decreasing the oxygen to 93 percent (from 95 percent) for the first 5 to 20 minutes of treatment. These investigators believed that 7 percent carbon dioxide gives a more satisfactory respiratory stimulation. No experimental or clinical evidence has been uncovered to demonstrate any damage from 7 percent carbon dioxide, and 300 cases of carbon monoxide poisoning treated with a mixture of 7 percent carbon dioxide and 93 percent oxygen for the first 5 to 20 minutes, completing the treatment with the usual 5 percent carbon dioxide-95 percent oxygen mixture, have shown good results. It is stated that breathing is more active and consciousness returns more quickly.

A case of attempted suicide with illuminating gas treated with good results by intravenous injection of 1 percent solution methylene blue was reported by Bell (*1785*) in 1933. However, Rossiter (*1707*) 1942 condemns the use of methylene blue, and also Thiel (*1794*) 1937 considers that injection of methylene blue may have harmful after-effects.

1785. Bell, M. A. Methylene blue in carbon monoxide poisoning. *J. Amer. med. Ass.*, 1933, *100:* 1402. [Ch]

1786. Drinker, C. K. and T. J. Shaughnessy. The use of 7 percent carbon dioxide and 93 percent oxygen in the treatment of carbon monoxide poisoning. *J. industr. Hyg.*, 1929, *11:* 301–314. [P]

1787. Haggard, H. W. and Y. Henderson. The treatment of carbon monoxide poisoning. *J. Amer. med. Ass.*, 1921, *77:* 1065–1068. [P]

1788. Henderson, Y. The dangers of carbon monoxide poisoning and measures to lessen these dangers. *J. Amer. med. Ass.*, 1930, *94:* 179–185. [P]

1789. Henderson, Y. Applications of the physiology of respiration to resuscitation from asphyxia and drowning and to the prevention and treatment of secondary pneumonia. *Yale J. Biol. Med.*, 1931–32, *4:* 429–436. [P]

1790. Henderson, Y. and H. W. Haggard. The treatment of carbon monoxid asphyxia by means of oxygen + CO_2 inhalation. A method for the rapid elimination of carbon monoxide from the blood. *J. Amer. med. Ass.*, 1922, *79:* 1137–1145. [P]

1791. Mosso, A. La mort apparente du coeur et les secours dans l'empoisonnement par l'oxyde de carbone. *Arch. ital. Biol.* 1901, *35:* 75–89. [P]

1792. Sayers, R. R. and H. R. O'Brien. The treatment of carbon monoxide poisoning. *Publ. Hlth Rep., Wash.*, 1922, no. 728: 271–274. [P]

1793. Sayers, R. R. and W. P. Yant. Dangers of and treatment for carbon monoxide poisoning. *Milit. Surg.*, 1925, *57:* 64–74. [P]

1794. Thiel, K. Ueber die Verwendung von Methylenblau bei der Behandlung der Kohlenoxydgasvergiftung. *Z. GewHyg.*, 1937, *44:* 23–25 [P]

(g) Detection of Carbon Monoxide in the Air and in the Blood

Methods for detection and determination of carbon monoxide in air and in blood need not be given in detail here. For a review of these methods, the reader is referred to Berger and Schrenk's report (*1795*) which appeared in 1938. The pyrotannic method is practical for air concentrations of 0.01 to 0.20 percent carbon monoxide. The Hoolamite or activated iodine pentoxide method provides a semiquantitative technique for estimating carbon monoxide concentrations from 0.10 to 1.0 percent. The ampule type carbon monoxide detector is described, and various recording devices are referred to. The use of the pyrotannic method for quantitative determination of carbon monoxide in the blood and in the air was described in 1927 by Sayers and Yant (*1797*). A paper by Henry (*1796*) on the analysis of confined air was published in 1918. The use of the response of Japanese waltzing mice and canaries to detect harmful amounts of carbon monoxide in air was reported by Yant, Patty, Schrenk, and Berger (*1799*) in 1930. It had been previously considered that Japanese waltzing mice might be useful to detect dangerous concentrations of carbon monoxide, since they are believed to be more susceptible to this gas than canaries, common house mice, or white mice because of their incessant activity. Mice and canaries are not significantly more susceptible to oxygen deficiency than man. The Japanese waltzing mouse appears to be as sensitive as the canary to concentrations of 0.2 to 0.24 percent carbon monoxide in air by volume, and more sensitive than canaries to concentrations of 0.14 to 0.16 percent carbon monoxide. Waltzing mice exposed to 0.10 to 0.12 percent carbon monoxide gave positive indications of poisoning in 5 to 10 minutes, while canaries generally failed to give indications after 75 to 131 minutes. Canaries are, therefore, unsatisfactory

as indicators in this lower range of concentration. At concentrations above 0.25 percent, the time margin between the undesirable effects on man doing moderate work and effects on either waltzing mice or canaries is narrow. Remarkably high individual tolerances are occasionally found among canaries. The sensitivity of animals to carbon monoxide in concentrations between 0.10 percent and 0.25 percent increases in the following order: white mice, canaries, and waltzing mice. It was concluded that waltzing mice and canaries are slightly more sensitive to carbon monoxide than man. The margin is not wide enough for either animal to be used as a practical detector for atmospheres dangerous to man.

1795. Berger, L. B. and H. H. Schrenk. Methods for the detection and determination of carbon monoxide. *Tech. Pap. Bur. Min., Wash.*, 1938, no. 582: 1–30. [P]

1796. Henry, [ ]. Analyse sur place de l'air confiné et des atmosphères suspectes. *Arch. Méd. Pharm. nav.*, 1918, *106:* 309–312. [P]

1797. Sayers, R. R. and W. P. Yant. The pyrotannic acid method for the quantitative determination of carbon monoxide in blood and in air. Its use in the diagnosis and investigation of cases of carbon monoxide poisoning. *Tech. Pap. Bur. Min., Wash.*, 1927, no. 373: 1–18. [P]

1798. Sendroy, J. and E. J. Fitzsimons. Determination of carbon monoxide in gas mixtures. *J. biol. Chem.*, 1944, *156:* 61–75. Abstr. *Bull. Hyg., Lond.*, 1945, *20:* 143. [P, M]

1799. Yant, W. P., F. A. Patty, H. H. Schrenk, and L. B. Berger. The response of Japanese waltzing mice and canaries to carbon monoxide and to atmospheres deficient in oxygen. *Rep. Invest. U.S. Bur. Min.*, 1930, no. 3040: 1–12 [P]

2. ARSENIURETTED HYDROGEN

Poisoning of submarine personnel by arseniuretted hydrogen is a hazard which is now largely of historical concern. This is true, however, only because of constant recognition of the danger and because of adequate precautions to protect the atmosphere from contamination with this highly toxic substance. It is, therefore, essential that medical officers responsible for the health of submarine crews or medical consultants concerned with problems of submarine design should be aware that arsenic may exist as an impurity in battery grids and battery acid and should insist upon the purity of these materials and upon rigid enforcement of adequate ventilation of battery compartments.

Two classical reports on arseniuretted hydrogen poisoning in submarines may be consulted, the first by Giordano (*1807*) published in 1917 and the second by Dudley (*1803, 1804*) which appeared in 1919. Giordano described symptoms and signs of intoxication in the crew of a certain Allied submarine which had gone out on a run in July 1917 and had remained continuously submerged for 16 hours. The symptoms from which the crew suffered were at the time attributed to the conditions of the atmosphere within the submarine. However, in August 1917 another submarine, after a continuous period of submergence of 15 hours, was compelled to return to its base with 17 out of its crew of 26 overcome by a toxic disorder not previously observed in submarine personnel except in a minor degree in the July incident. During the run, the sea had been calm. However, new batteries had just been installed, and the trial dive had lasted only 6 hours. The batteries were located in the after compartment and the ventilating system was so arranged that air was driven by blowers from this compartment in a forward direction. The oxygen concentration was determined to be ample, the temperature within normal limits, and the pressure not higher than 8 mm. Hg above 1 atmosphere. All 17 of the men affected had been in the forward compartment. The first case of illness occurred after 9 hours of submergence; 2 further crewmen became ill after 12 hours; 4 men were attacked after 14 hours; and the rest of the cases developed on surfacing. The symptoms were similar in every instance: nausea, vomiting, malaise, a burning sensation of the throat, a metallic taste in the mouth, intestinal griping, diarrhea, headache, vertigo, and weakness. The second day after onset, all patients had jaundice which lasted for 48 hours or more, and in 1 case, the patient was icteric for 12 days. Headache, insomnia, and anorexia lasted for 2 or 3 days. In 2 cases, the burning in the pharynx lasted for 2 days. The stools were first liquid, and then chalky and pale. There was tenderness over the liver, with slight enlargement in some cases. There were

marked psychic effects. All patients showed fairly complete recovery within 15 days, being left only with weakness and lassitude. Urobilin and traces of bilirubin and, in some cases, blood were present in the urine. There was a marked anemia, the blood count having fallen to about 3 million red cells per cubic mm. The hemoglobin values lay between 60 and 70. Corpuscular resistance, as measured by the Ribierre method, was 0.26 to 0.30, an increase above normal. The white blood count lay between 6,000 and 7,200, and the serum was yellowish to red. There was marked poikilocytosis with many dwarf red cells and macrocytes. A few nucleated red cells were seen.

In a third submarine, an identical accident occurred. On 2 dives on August 23 lasting 10 and 15 hours respectively, the entire personnel suffered the same symptoms and signs as were observed in the submarine incident of August of the same year, cited above. The disturbances were, however, somewhat less severe. In both submarines, the batteries had just been renewed. These batteries were of the type not provided with airtight covers or openings for ventilation, but were in direct communication with the surrounding air. The lead plates in the batteries were enveloped in bags made of asbestos to prevent the crystals of PbO_2, which form on the positive plates, from falling to the bottom as a result of the boat's movements. Analysis of the batteries revealed the presence of arsenic in the asbestos and traces of arseniuretted hydrogen in the surrounding air when the batteries were in operation. There seemed no doubt, therefore, that the illnesses of personnel were due to the poisonous effects of arseniuretted hydrogen evolved from the batteries during charging, and that the arsenic was present as an impurity in the new asbestos bags. After the batteries had been repeatedly charged and discharged, dogs, rabbits, and pigeons were enclosed in the compartment containing the batteries. Since no ill effects followed this test, the submarines were ordered back to their regular stations.

Dudley (*1804*) 1919 reported that on 15 June 1916, 3 men from the submarine *D-4* were admitted to the Royal Naval Hospital, Chatham, diagnosed as having carbon monoxide or carbon dioxide poisoning. All suffered from gross destruction of red cells. These were actually cases of poisoning by arseniuretted hydrogen. The submarine *D-4* made 2 trips during which the illnesses occurred. The first trip started 16 May 1916 and the submarine was absent from base for 7 days, making daily submergences, each lasting about 17 hours. The submarine returned to the base on 24 May. The second trip started on 3 June, lasting for 4 days, the boat being forced to return on 8 June because of illness of the crew. The average time of submergence each day was 17 hours. Another submarine, the *D-3*, made 3 trips during which symptoms developed. The third trip was an experimental run for the purpose of studying toxic effects. On return, the submarine commander stated that the first symptoms started at the eighth hour of the dive. There was vomiting on the fourteenth hour and at the eighteenth hour, the submarine broke surface. Within 20 minutes after surfacing, 20 out of a crew of 26 had vomited. This third trip of submarine *D-3* conclusively demonstrated that the batteries were the source of the gas. In all, 30 cases of arseniuretted hydrogen poisoning were admitted from the 2 boats (*D-3* and *D-4*), 15 from each. The symptomatology as exhibited in the cases from these boats has been summarized in carefully compiled tables in Dudley's report. The temperature of patients was nearly always normal on admission to hospital while the pulse rate tended to be elevated. Dyspnea was a general symptom, particularly on exertion, and was evidently due to acute anemia, since there were no pulmonary signs whatever. Vomiting was a constant feature. Patients usually suffered from constipation, but some had diarrhea, and there was 1 case with bloody stools. The urine was brown to blood red, blood pigments or blood itself being found on analysis. Albuminuria was present at one time or other in all but 3 cases. Edema of the face and eyelids was observed in several patients while aboard the submarine, but there was no involvement of the feet and ankles. Dudley believed that this indicated

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the presence of a toxic nephritis. In some cases, there was conjunctivitis, probably due to irritation by arsenic in the blood stream. Headache and insomnia were frequent symptoms, and may well have been secondary to the nephritis. In all but 4 cases, there was peripheral neuritis. This was not usually manifest until 3 to 4 days after return from the voyage, and persisted 2 to 3 weeks. Patients complained of tingling, numbness, and "pins and needles" in the hands and feet. Some had shooting pains in the legs, back, and shoulders. About one-half of the victims complained of toothache or facial neuralgias. There were no changes in the reflexes, or any sensory anesthesia. Jaundice was a constant sign.

Nearly 200 complete blood counts and hemoglobin estimations were made. In all patients, the red blood count was below 5 million cells per cu. mm., 2 being below 2 million. In 12 cases, the count was between 2 and 3 million red cells per cu. mm. In 10, it was between 3 and 4 million. In 6 patients, the count was over 4 million. The lowest count in any patient was 1,780,000. In the second month, the red blood count tended to return to normal. The white blood count showed little or no difference from normal but the hemoglobin concentration was reduced in all cases. There was usually a high color index. The differential white count showed nothing very characteristic, but patients generally showed relative and actual lymphocytosis. Eosinophile leucocytes were increased above normal in many cases. The red cells showed normal appearance in most instances. There was poikilocytosis as well as basophilic staining and in some cases punctate basophilic stippling. There was a tendency toward decreased fragility of red cells. The Arneth count showed a definite toxic "drift to the left," that is to say, a relative increase in the number of polymorphonuclear leucocytes with fewer differentiations in their nuclei. The urine was examined in 18 cases and only 3 gave positive results for arsenic. However, these were the only 3 cases in which the urine was tested within less than a week after leaving the submarine. Arsenic was detected in the combined nail parings from 10 cases (Reinsch test). The hair was also positive to the Reinsch test. Dudley considered that arseniuretted hydrogen probably does not have a direct, destructive action on blood cells, but that it damages and alters the contents of the erythrocytes, and that these altered red cells are then destroyed in the liver. The main features of the submarine cases are similar to those of acute industrial arseniuretted hydrogen poisoning, except that none of Dudley's cases showed rigors. Albuminuria or neuritic symptoms are mentioned by certain authors describing cases of industrial poisoning. Mann, quoted by Dudley, reported a mortality of 36.7 percent in his cases. The submarine cases were more chronic or sub-acute than Mann's cases.

Regarding the source of the arseniuretted hydrogen, the batteries in the submarines in question had been in use for over 5 years. The hydrochloric acid was free of arsenic, but examination of the metallic portion of the battery plates showed a concentration of 0.2 percent arsenic, and this proved to be the source of poisoning. At the time the grids were made, antimonial lead alloy was used. The original surface had been deeply corroded, the effect of which was slowly to convert the metallic lead in the alloy into insoluble lead peroxide and to permit arsenic to pass into solution. The rate at which the arsenic became dissolved would at first be negligible until the gassing period was reached. At this point, the impurities in the electrolyte, assisted by electro-chemical action, would dissolve the arsenic exposed by the corrosive action on the alloy. The arsenic dissolved in the electrolyte would be carried to the negative electrode in small amounts as dissolved and there converted into arseniuretted hydrogen. In the newer batteries, such as those installed in British submarines of Class E, the grid castings were made of an alloy of lead and pure antimony, instead of antimonial lead alloy. Dudley pointed out that in more recent years, antimony of high purity had become available commercially. Therefore, a repetition of the trouble was not expected.

One of the best reference works on arsen-

iuretted hydrogen poisoning is the monograph by Glaister (*1808*) published in 1908. This valuable work records observations on 120 cases of arsene poisoning. It contains a well-selected bibliography of 47 items. The properties and sources of arsene and its relation to scientific and industrial operations are given and symptoms are described in detail. The clinical picture is not characteristic of this particular form of poisoning alone. Symptoms arise actually from the widespread destruction of red blood cells, and therefore are characteristic of any hemolytic anemia. According to Glaister, symptoms appeared within a few minutes to 24 hours, the average time of onset being 3 to 6 hours. The time of onset depends upon the percentage concentration of the gas in the atmosphere and the condition of the individual at the time of exposure. Glaister points out that there may be individual variability of symptoms, but that the early symptoms are usually an indefinable feeling of illness and great weakness, giddiness, pains in the head and epigastrium, coldness of the body, a sense of oppression of breathing accompanied in some cases by cyanosis, nausea, and vomiting. Vomiting then usually becomes a more pronounced feature with emesis first of bile, then of bloody material. The patient becomes jaundiced, the color varying from a golden yellow to a mahogany or copper tint. The color is usually generalized over the body, but may be present only in the conjunctivae. There is thirst, dryness in the throat, weakness of the voice, pains in the loins and over the region of the liver. There may be hemoglobinuria, hematuria, oliguria, and in fatal cases, coma with or without delirium. Hiccough and subnormal temperature are encountered, usually toward the end. The area of liver and spleen dullness is enlarged in most cases.

The clinical picture, as has been said, depends upon a rapid hemolysis with resulting incapacity of the blood adequately to tranport oxygen, and inability of the body to cope with the elimination of the destroyed red cells. In 120 cases recorded from time to time in various journals, the fatality rate was 31.36 percent. The minimum period of survival was 2 days and the maximum, 30 days. On post-mortem examination, there was jaundice and a blue line on the margin of the gums and teeth as in lead poisoning. The meninges are anemic, edematous, or the dura may be anemic and the pia-arachnoid congested. The brain substance is usually pale and anemic and in some cases may have an icteric coloration. The lungs are generally collapsed and congested, the congestion being usually confined to the lower lobes. There may be fatty degeneration of the myocardium and this may be a proximate cause of death. The liver is more or less swollen and enlarged due to engorgement of the tissue from biliary stasis and deposition of blood pigment. Microscopically, there are deposits of brown-colored pigment in the hepatic cells, especially in the vicinity of the hepatic veins. There is cloudy swelling of the hepatic cells and also fatty degeneration. Similar pigment deposits are seen in the cellular structure of the heart, kidney, and intestines. The liver is usually yellow, grayish-brown, yellowish-brown, or greenish-yellow, or may be slate blue or even deep indigo. The gall bladder is full of dark bile, and the kidneys are hyperemic and vary in color from dark red or brown to brownish-black, violet, or indigo. The glomeruli are swollen and the epithelial lining of Bowman's capsule may be detached or in a condition of proliferation and swelling. The tubules are more or less full of broken-down corpuscles and in a state of desquamative inflammation. The spleen is sometimes swollen, but often normal in size. It is usually soft, friable, and congested. The color is brownish-red to blue. The stomach and intestines are hyperemic, and petechial mucous hemorrhages are to be seen.

Glaister (*1808*) described the symptoms and post-mortem appearances produced experimentally in animals by administration of arseniuretted hydrogen. He also discussed differential diagnosis. Treatment and prevention were also considered, as well as the methods of detection of arsenic. Detailed reports of 7 of the author's cases and 40 other cases are given. Some of the data discussed in

Glaister's monograph are included in a paper (*1809*) which he published in 1913.

The reader may consult an article by Legge (*1815*) published in 1924 for a general discussion of arseniuretted hydrogen poisoning in industrial occupations. Kober (*1812*) in 1924 refers to a number of earlier case reports of particular interest. One report described individuals who were poisoned in filling toy balloons with hydrogen contaminated by arseniuretted hydrogen. A case history is also given by Ollivier (*1819*) 1863 in which death occurred in 4 days. Several cases are cited by Eitner (*1806*) 1880, and acute fatal cases were described by Coester (*1802*) in 1884.

A case of particular interest was that described by Schickhardt (*1821*) in 1891 of acute arseniuretted hydrogen poisoning in a German chemist. This patient was exposed to arseniuretted hydrogen generated by the action of glacial acetic acid on zinc containing arsenic as an impurity. Fortunately, the patient recovered in 10 days after showing an acute picture.

In 1900, Maljean (*1817*) described the case of 3 military personnel poisoned by arseniuretted hydrogen present as an impurity in hydrogen gas used in filling military balloons. The patients in question worked in the inflation hangar and all 3 recovered. These cases are also discussed by Granjux (*1810*) 1900 and Durand (*1805*) in 1900. Ten cases of poisoning were reported by Clayton (*1801*) in 1901, and a report of 5 cases was given by Jones (*1811*) in 1907. In 1920, Wignall (*1824*) described 5 case histories. The author believed that arsenic could be excreted in the urine without the patient's showing any symptoms. A report on the clinical course of 11 acute arseniuretted hydrogen cases was given by Löning (*1816*) in 1931, while Bomford and Hunter (*1800*) 1932 reported 2 cases of arseniuretted hydrogen poisoning due to the action of water poured on hot dross containing arsenic in a tin refinery. For other reports on arseniuretted hydrogen poisoning, the reader may consult papers by Tcherkess, Rosovsky, and Sila (*1822*) 1935; Rabuteau (*1820*) 1873; Labes (*1814*) 1926: the U. S. Department of Labor, Division of Labor Standards (*1823*) 1939; Mann and Clegg (*1818*) 1895; and Koelsch (*1813*) 1920. Concerning the mechanism of the toxic action of arseniuretted hydrogen, Rabuteau carried out experiments on the effect of arsene on defibrinated blood *in vitro*. Labes stated that arsene had no harmful effect upon oxygen-free red blood cells *in vitro* and believed that the toxicity of the gas was due to its oxidation to colloidal arsenic by blood oxygen with subsequent hemolysis of the cells.

1800. Bomford, R. R. and D. Hunter. Arseniuretted hydrogen poisoning due to the action of water on metallic arsenides. *Lancet*, 1932, *2:* 1446–1449 [R, Ch]

1801. Clayton, J. S. A report on ten cases of poisoning by arsenetted hydrogen. *Brit. med. J.*, 1901, *1:* 392–393. [Ch]

1802. Coester, [ ]. Vergiftung durch Arsenwasserstoffgas mit tödtlichem Ausgang (Haemoglobinurie, Icterus, Anurie). *Berl. klin. Wschr.*, 1884, *21:* 119–121. [Ch]

1803. Dudley, S. F. Arseniuretted hydrogen poisoning in submarines. *J. R. nav. med. Serv.*, 1919, *5:* 239–248 [Ch]

1804. Dudley, S. F. Toxemic anemia from arseniuretted hydrogen gas in submarines. *J. industr. Hyg.*, 1919, *1:* 215–232. [Ch, R]

1805. Durand, [ ]. Intoxication des aérostiers par l'hydrogène arsénié. *Ann. Hyg. publ. Paris*, 1900, Sér. 3, *44:* 35–38. [Ch]

1806. Eitner, [ ]. Mehrere Fälle von Haemoglobinurie, hervorgerufen durch Einathmen von Arsenik-Wasserstoffgas. *Berl. klin. Wschr.*, 1880, *17:* 256–257, [Ch]

1807. Giordano, M. Poisoning by arseniuretted hydrogen on submarines. *Nav. med. Bull., Wash.*, 1917, *11:* 342–346. [Ch]

1808. Glaister, John. *Poisoning by arseniuretted hydrogen or hydrogen arsenide. Its properties, sources, relations to scientific and industrial operations, symptoms, postmortem appearances, treatment, & prevention; with a record of one hundred and twenty cases by different observers.* Edinburgh, E.&S. Livingstone, 1908, ix, 279 pp. [R]

1809. Glaister, J. Poisoning by arseniuretted hydrogen and arsenical fumes from scientific and industrial operations. *Int. Congr. Med.*, (XVII Congr., London), 1913, (Sect. 19, Forensic Medcine. Part 2): 139–152. [R]

1810. Granjux, [ ]. Intoxication des aérostiers par l'hydrogène arsenié. *Bull. méd., Paris*, 1900, *14:* 354–355 [Ch]

1811. Jones, N. W. Arseniuretted hydrogen poisoning. With report of five cases. *J. Amer. med. Ass.*, 1907, *48:* 1099–1105. [R, Ch]

1812. Kober, G. M. Peculiarities in arsenic poisoning. Pp. 315–320 in: *Industrial health.* Edited by George M. Kober and Emery R. Hayhurst. Philadelphia, P. Blakiston's Son & Co., 1924, lxxii, 1184 pp. [R]

1813. Koelsch, F. Gewerbliche Vergiftungen durch Arsenwasserstoff. *Zbl. GewHyg.*, 1920, *8:* 121–126. [R]

1814. Labes, R. Der Mechanismus der Arsenwasserstoffvergiftung. Ein Beitrag zum chemischen Verständnis der pharmakologischen Wirkung anorganischer Arsen- und ähnlicher Verbindungen. *Dtsch. med-Wschr.*, 1926, *52:* 2152–2154; 2192–2193. [R]

1815. Legge, T. M. Arsenic poisoning. Pp. 303-314 in: *Industrial health.* Edited by George M. Kober and Emery R. Hayhurst. Philadelphia, P. Blakiston's Son & Co., 1924, lxxii, 1184 pp. [R]

1816. Löning, F. Klinischer Bericht über den Verlauf von elf akuten AsH_3-Vergiftungen. *Zbl. inn. Med.*, 1931, *52:* 833–837. [Ch]

1817. Maljean, [ ]. Intoxication par le gaz hydrogène arsénié chez les aérostiers. *Arch. Méd. Pharm. milit.*, 1900, *35:* 82–102. [Ch]

1818. Mann, J. D. and J. G. Clegg. On the toxic action of arsenetted hydrogen, illustrated by five cases. *Med. Chron.*, 1895, N. ser., *3:* 161–171. [Ch]

1819. Ollivier, A. Observation d'empoisonnement par l'hydrogène arsénié. *C. R. Soc. Biol. Paris*, 1863, Sér. 3, *5:* 77–80. [Ch]

1820. Rabuteau, [ ]. Sur le méchanisme de l'intoxication arsenicale et l'action de l'hydrogène arsenié sur le sang. *C. R. Soc. Biol. Paris*, 1873, *5:* 153–155.

1821. Schickhardt, [ ]. Ein Fall von Arsen-Wasserstoff-Vergiftung. *Münch. med. Wschr.*, 1891, *38:* 26–27. [R, Ch]

1822. Tcherkess, A. I., E. S. Rosovsky, and B. I. Sila. (L'anoxémie dans le mécanisme d'intoxication par les poisons du type hemolytique (l'hydrogène arsénic).) *Eksper. Med., Kharkov*, 1935, no. *3:* 21–32. (With Russian and French summaries.)

1823. U. S. Department of Labor. Division of labor standards. *The causes and prevention of arsenic poisoning.* Industrial health series no. 3. Washington, D. C., Govt. print. off., 1939, 4 pp. [R]

1824. Wignall, T. H. Poisoning by arseniuretted hydrogen. *Brit. med. J.*, 1920, *1:* 826–827. [Ch]

3. OTHER NOXIOUS GASES

If allowed to accumulate in sufficient quantities, hydrogen liberated from the storage batteries may constitute an explosion hazard. Hydrogen explosions were described in an unsigned article (*1835*) published in 1924 in the Naval Medical Bulletin.

Poisoning by various gases liberated from the muck in caissons has been reported by Barrat and Seigner (*1825*) 1936. They stated that caisson workers complained of general intoxication, headache, vertigo, vomiting, acute coryza, and hyperemia of the conjunctiva from working in an atmosphere containing gas from putrifying marine organisms. The gases involved were probably hydrogen sulfide and organic sulfur-containing compounds.

For a more detailed discussion of hydrogen sulfide poisoning, the reader may consult a report by the U. S. Department of Labor, Division of Labor Standards (*1834*) published in 1940. It appears that hydrogen sulfide was the gas responsible for fatalities occurring at Pearl Harbor in connection with the salvage of sunken and damaged ships as reported by Parker (*1831*) in 1944. In these operations, the ships in question lay in sewage-polluted water. Gases from a closed compartment caused 1 immediate death and 4 deaths 2 days later from hypostatic pneumonia. No abnormality was found in the blood, so carbon monoxide appears to have been ruled out. A concentration of 700 parts per million of hydrogen sulfide is considered sufficient to cause death within a short time and 1,000 parts per million may be instantly fatal. The victims complained of irritation of the mucous membranes, eyes, nose, and respiratory tract, burning of the throat, general signs of bronchitis, headache, dizziness, disturbances of the gastrointestinal tract, fatiguability, slow pulse, irritability, and certain psychic disorders such as inability to concentrate. The author formulated general rules for testing gas concentrations in ships being salvaged. These rules may be applicable in the salvaging of submarines. Parker emphasized the importance of removing toxic gases by suction ventilation and stated that an apparatus for the administration of 95 percent oxygen and 5 percent carbon dioxide should be available for rescue work. Personnel testing for gases should be equipped with breathing apparatus and suitable clothing to cope with oil, muck, and mire.

In 1939, Dorello (*1827*) reported on methyl chloride poisoning in an Italian submarine. This substance was used in the cooling system and by accident became liberated in the atmosphere. The victim suffered from slow, soft, small pulse, exaggeration of the deep

reflexes, tendency to mydriasis, sluggish pupillary reflexes, and marked pallor of the skin and mucosa.

Patti (*1832*) 1939 reported on phosphine poisoning on a submarine. Other toxic substances such as phosgene, carbon dioxide, etc., have been considered in reports by Lehmann (*1830*) 1886; Fairlie (*1828*) 1920; Piéry, Chambon, and Périer (*1833*) 1937; and Derrick and Johnson (*1826*) 1943.

1825. Barrat, P. and A. Seigner. Une maladie professionnelle peu connue: intoxication par gaz provenant de certains fonds sous-marins chez des ouvriers travaillant dans les cloches à plongeur. *Ann. Oculist., Paris*, 1936, *173:* 513–528. [R]

1826. Derrick, E. H. and D. W. Johnson. Three cases of poisoning by irrespirable gases: phosgene from trichlorethylene, nitrogen dioxide, carbon dioxide with reduction of oxygen. *Med. J. Aust.*, 1943, *2:* 355–358. [P, Ch]

1827. Dorello, F. Su di un caso di intossicazione collettiva a bordo di un sommergibile (da cloruro di metile). *Ann. Med. nav. colon.*, 1939, *45:* 37–46. [Ch]

1828. Fairlie, W. M. Poisoning by nitrous gases. *J. R. nav. med. Serv.*, 1920, *6:* 66–76. [R]

1829. Gréhant, N. Analyse de l'air des mines. *Pr. méd.*, 1906, *14:* 183.

1830. Lehmann, K. B. Experimentelle Studien über den Einfluss technisch und hygienisch wichtiger Gase und Dämpfe auf den Organismus. (Theil I und II: Ammoniak und Salzsäuregas.) *Arch. Hyg., Berl.*, 1886, *5:* 1–126. [R]

1831. Parker, C. M. Gases in sunken and damaged ships. *Nav. med. Bull., Wash.*, 1944, *42:* 743–747. [R]

1832. Patti, M. Intossicazione collettiva da idrogeno fosforato gassoso (PH_3) a bordo di un sommergibile. *Ann. Med. nav. colon.*, 1939, *45:* 432–438.

1833. Piéry, M., M. Chambon, and E. Périer. Etude de la dépression atmosphérique sur l'animal intoxiqué au phosgène. *C. R. Soc. Biol. Paris*, 1937, *126:* 20–21. [P]

1834. U. S. Department of Labor. Division of Labor Standards. *The causes and prevention of hydrogen sulphide poisoning.* Industrial health series no. 19. Washington, D. C., Govt. print. off., 1940, 5 pp. [R]

1835. Anon. Explosion hazards, storage batteries in submarines. *Nav. med. Bull., Wash.*, 1924, *21:* 137–139.

C. ORGANIC SOLVENTS

1. GASOLINE AND BENZENE POISONING

Chronic exposure to benzene may be encountered under certain conditions in submarines or compressed air works. According to Bowditch and Elkins (*1836*) 1939, 75 parts per million of benzene vapor in the air is probably the maximum safe concentration, although a concentration of 100 parts per million is the commonly accepted value. The clinical effects of chronic benzene poisoning have been discussed by Hunter (*1841*) 1939 and the pathological effects by Mallory, Gall, and Brickley (*1843*) 1939. There may be severe blood changes, such as increase or decrease in the red blood cell count, leucocytosis, eosinophilia, or leucopenia. Splenic enlargement is frequently present and the bone marrow may show complete aplasia or bizarre hyperplasia. Patients have muscular cramps, dyspnea on exertion, and loss of appetite. The first signs of poisoning may appear with the onset of an infection. Hunter believed that any concentration of benzene inhaled over a long period of time might be dangerous.

Histological material from 19 patients with a history of chronic exposure to benzene (14 autopsies and 5 biopsies) was described and analyzed by Mallory, Gall, and Brickley (*1843*). The entire hematopoietic system showed severe changes. The red bone marrow varied from severe hypoplasia to extreme overactivity. Extra-medullary hematopoiesis also occurred. Contrary to the prevailing opinion, the authors found hyperplasia to be the more common of the 2 reactions. Hyperplasia was found only in those patients with prolonged exposure but hypoplasia might be present in either long or short exposure cases. In certain hyperplastic areas, hematopoeitic elements were so atypical as to be distinguishable from neoplasia only with difficulty.

In cases of chronic benzol poisoning in the rotogravure printing industry in New York, Greenberg, Mayers, Goldwater, and Smith (*1840*) 1939 observed a drop in the red blood count to less than 4,500,000 in 47.8 percent of 150 persons examined. A reduction of blood platelets to less than 100,000 per cu. mm. occurred in 32.7 percent of 107 studied while in 15.3 percent of 235 persons, there was a reduction of hemoglobin to less than 13 grams per hundred cc. The white blood cell count was reduced to less than 5,000 per cu. mm. in 14.5 percent of 332 persons examined. In-

creased bilirubin values were detected in approximately 33 percent of 102 cases studied. Serious abnormalities in the blood picture were encountered in the absence of signs and symptoms. The blood picture in benzol poisoning was discussed by Erf and Rhoads (*1838*) in 1939.

Yant, Schrenk, and Patty (*1847*) 1936 discussed urine sulfate determinations as a measure of benzene exposure. The comparative physiological effects of pure commercial and crude benzenes were discussed in 1940 by Schrenk, Yant, Pearce, and Sayers (*1844*).

For a study in gasoline intoxication, the reader may consult a paper by Machle (*1842*) published in 1941. This report contains a good bibliography and describes the pathological symptomatology, laboratory findings, sequelae, and therapy of this condition. The toxicity of benzene, toluene, xylene, gasoline, and naphtha was discussed in 1943 in a paper by Carlyle (*1837*). Other papers which may be consulted on benzol poisoning are those by Gaulejac and Dervillée (*1839*) 1938; Störring (*1845*) 1940; and U. S. Department of Labor, Division of Labor Standards (*1846*) 1943. A report by Fulton and Hoff, previously referred to (*1702*), may be consulted for a brief statement of the problems of the toxic effects of gasoline in aircraft.

1836. Bowditch, M. and H. B. Elkins. Chronic exposure to benzene (benzol). I. The industrial aspects. *J. industr. Hyg.*, 1939, *21:* 321–330. [R]

1837. Carlisle, J. M. The toxicity of certain organic solvents in industry. Pp. 256–268 in: *The principles and practice of industrial medicine.* Edited by Fred J. Wampler. Baltimore, The Williams & Wilkins Company, 1943, xiv, 579 pp. [R]

1838. Erf, L. A. and C. P. Rhoads. The hematological effects of benzene (benzol) poisoning. *J. industr. Hyg.*, 1939, *21:* 421–435. [B, Ch]

1839. Gaulejac, R. de and P. Dervillée. Les dangers d'intoxication résultant de l'emploi du benzol comme carburant, particulièrement dans les formations aériennes; mesures préventives. *Ann. Méd. lég.*, 1938, *18:* 152–156.

1840. Greenburg, L., M. R. Mayers, L. Goldwater, and A. R. Smith. Benzene (benzol) poisoning in the rotogravure printing industry in New York City. *J. industr. Hyg.*, 1939, *21:* 395–420. [Ch]

1841. Hunter, F. T. Chronic exposure to benzene (benzol). II. The clinical effects. *J. industr. Hyg.*, 1939, *21:* 331–354. [R]

1842. Machle, W. Gasoline intoxication. *J. Amer. med. Ass.*, 1941, *117:* 1965–1971. [R]

1843. Mallory, T. B., E. A. Gall, and W. J. Brickley. Chronic exposure to benzene (benzol). III. The pathologic results. *J. industr. Hyg.*, 1939, *21:* 355–393. [R]

1844. Schrenk, H. H., W. P. Yant, S. J. Pearce, and R. R. Sayers. Comparative physiological effects of pure commercial and crude benzenes. *J. industr. Hyg.*, 1940, *22:* 53–63.

1845*. Störring, E. Über Vergiftungen mit Flugbenzin. *Luftfahrtmed. Abh.*, 1940, *3:* 35–36.

1846. U. S. Department of Labor. Division of Labor Standards. *Benzol (benzene) poisoning. Cause and prevention.* Industrial health series no. 8. Washington, D. C., Govt. print. off., 1943, 5 pp. [R]

1847. Yant, W. P., H. H. Schrenk, and F. A. Patty. A plant study of urine sulfate determinations as a measure of benzene exposure. *J. industr. Hyg.*, 1936, *18:* 349–356. [P]

2. CARBON TETRACHLORIDE

Carbon tetrachloride may be a cause of poisoning in submarine personnel as well as in other occupations. For a description of symptoms and treatment, the reader is referred to a paper published in 1934 by Davis (*1848*). Cases of nephrosis due to carbon tetrachloride were described by Smetana (*1853*) 1939. Perry (*1850*) in 1942 presented a description of carbon tetrachloride poisoning based on 88 cases. The victims were soldiers who were exposed to the toxic fumes of carbon tetrachloride while cleaning newly-issued rifles in a barracks room. Five required hospitalization and 2 died. The symptoms and clinical course were described. The narcotic action and secondary toxic effects of carbon tetrachloride were reviewed by Easton (*1849*) in 1943 and carbon tetrachloride poisoning in U. S. naval personnel was described by Sanford (*1851*) in 1943. Sanford reported the case of a young seaman who had been cleaning Diesel engine parts. He used a bottle of carbon tetrachloride to remove the oil and grime from his hands and forearms. He also cleaned his shoes with the solvent. He had supper and took a shower bath. He was then seen to stagger to his bunk where he collapsed and died within a few minutes in spite of artificial respiration and other restorative measures. It is possible that in this case, the finely divided metal and grime on his hands may have changed the carbon tetrachloride

to phosgene and that this was, in fact, the cause of the poisoning.

Poisoning by chlorinated solvents was discussed in a report published in 1943 by the U. S. Department of Labor, Division of Labor Standards (*1846*), and Sherman and Binder (*1852*) in a report published in 1944 discussed the toxicology of carbon tetrachloride poisoning together with case histories and method of treatment.

1848. Davis, P. A. Carbon tetrachloride as an industrial hazard. *J. Amer. med. Ass.*, 1934, *103:* 962–966. [R]

1849. Easton, W. H. Carbon tetrachloride—in industrial hygiene. *Industr. Med.*, 1943, *12:* 1–3. [B, R]

1850. Perry, W. J. Carbon tetrachloride poisoning: a report of eighty-eight cases. *Army med. Bull.*, 1942, *64:* 70–74. [M, Ch]

1851. Sanford, S. P. Carbon tetrachloride poisoning. *Nav. med. Bull., Wash.*, 1943, *41:* 1486–1488. [M, Ch]

1852. Sherman, S. R. and C. F. Binder. Hazards of carbon tetrachloride in present-day use. *Nav. med. Bull., Wash.*, 1944, *43:* 590–599. [Ch]

1853. Smetana, H. Nephrosis due to carbon tetrachloride. *Arch. intern. Med.*, 1939, *63:* 760–777. [B, R]

1854. U. S. Department of Labor. Division of Labor Standards. *Poisoning by chlorinated solvents. Cause and prevention.* Industrial health series no. 11. Washington, D. C., Govt. print. off., 1943, 4 pp. [R]

3. OTHER ORGANIC SOLVENTS

Papers which may be consulted for information on volatile solvents are reports by McConnell (*1855*) 1937; U. S. Department of Labor, Division of Labor Standards (*1857*) 1937; and Smythe (*1856*) 1944.

1855. McConnell, W. J. Volatile solvents as a problem in industrial medicine. *J. Amer. med. Ass.*, 1937, *109:* 762–768. [R]

1856. Smyth, H. F., Jr. Solvents and volatile organic materials. Pp. 123–138 in: *Introduction to Industrial Medicine.* Edited by T. Lyle Hazlett. Pittsburgh, University of Pittsburgh, 1944, 216 pp. [R]

1857. U. S. Department of Labor. Division of Labor Standards. *Carbon bisulphide poisoning (carbon disulphide). Its cause and prevention.* Industrial health and safety series no. 12. Washington, D. C., Govt. print. off., 1937, 4 pp. [R]

D. OTHER NOXIOUS AGENTS

A miscellaneous group of reports dealing with various noxious agents of interest to submarine medical officers is listed below: A paper by Guttmann (*1858*) published in 1878 may be consulted for an early account of sulfuric acid poisoning. Jones' report (*1860*) in 1939 discusses the injurious effects of and prevention of metal fumes; reports by Łuczak (*1861*) 1939 and Savcov (*1862*) 1940 are concerned with tetraethyl lead poisoning. Iacobelli (*1859*) in 1940 published a report of several cases of mercury poisoning aboard an Italian submarine.

1858. Guttmann, M. Vergiftung durch Schwefelsäure. *Wien. med. Pr.*, 1878, *19:* 153–154. [R, Ch]

1859. Iacobelli, G. Intossicazione collettiva da mercurio a bordo di un sommergibile. *Ann. Med. nav. colon.*, 1940, *46:* 465–469. [M]

1860. Jones, R. R. Metal fumes. Injurious effects and how to prevent them. *Nav. med. Bull., Wash.*, 1939, *37:* 507–516. [R]

1861. Łuczak, A. Czteroetylek ołowiv. (Plomb tétra éthyle.) *Polsk. Przegl. Med. Lotn.*, 1939, *8:* 135–145.

1862*. Savcov, S. I. (Sanitäre Sicherung der Arbeit mit Äthylfluid und Bleibenzin.) *Vo.-sanit. Dyelo*, 1940, no. 7: 52–55.

VII. ACCIDENTS IN SEALED COMPARTMENTS

Fatalities have been reported in personnel who entered sealed compartments in which the concentration of oxygen had fallen below a level capable of supporting life and in which there was a high concentration of carbon monoxide. Although these accidents have occurred for the most part in ships' compartments previously painted with linseed oil paint and sealed up, and although such accidents are not encountered in submarines, the brief literature is nevertheless reviewed here because of its relation to problems of ventilation, oxygen-lack, and the toxic effect of carbon monoxide. Readers should also consult the sections on the physiological effects of low oxygen and high carbon dioxide content of the environmental air (p. 51), carbon monoxide (p. 196), and ventilation (p. 244).

As Belli (*1863*) 1904 has shown, the concentration of oxygen in double bottoms of ships

can fall to very low levels. In one ship, air samples in such compartments showed oxygen concentrations ranging from 8.5 to 3.1 percent, while in various parts of the double bottom of another ship, the oxygen concentration varied between 2.4 to 2.2 percent. Referring to irrespirable air in sealed compartments of ships, Giemsa (*1868*) 1906 alluded to nitrogen "drowning" and carbon monoxide poisoning as causes of death. Newington (*1872*) 1931 reported a fatality due to entry into a sealed compartment that had been painted 5 years before and closed while the paint was still wet. The carbon monoxide present in the air of the ship's compartment was emitted during the drying of the linseed oil in the iron oxide paint. It was determined that carbon monoxide was produced in the process of drying of both boiled and raw linseed oil. The amount of carbon monoxide produced depends upon the amount of oxygen present for absorption by the oil; the maximum carbon monoxide concentration to be expected would be about 0.3 to 0.4 percent.

Investigations of the production of carbon monoxide from paint in sealed compartments by Dudding, Dudley, and Frederick (*1864*) 1931 and Dudley, Edmed, and Frederick (*1865*) 1933 indicated that iron oxide paint, red lead paint, and aluminum paint, all containing linseed oil, produced carbon monoxide and absorbed oxygen when painted on the walls of a sealed container.

Where the concentration of oxygen in a sealed compartment is very low, death is due to suffocation in nitrogen even though carbon monoxide may also be present, since there is not sufficient time for carbon monoxide poisoning. If the compartment is partially ventilated, there may be enough oxygen to permit survival until the victim is overcome by carbon monoxide present in dangerous concentrations in the air of the compartment. Great stress must, therefore, be laid upon the necessity of thorough ventilation of such compartments before entry.

Further references to the emission of carbon monoxide and absorption of oxygen during the drying of paint by the following authors may be consulted: Gardner (*1867*) 1914, King (*1870*) 1915, Klein (*1871*) 1915, and Flagg (*1866*) 1944.

1863. Belli, C. M. L'alterazione dell'aria nei doppii fondi delle navi. *Ann. Med. nav. colon.*, 1904, *1:* 293-302. [P]

1864. Dudding, J. S., S. F. Dudley, and R. C. Frederick. The production of carbon monoxide from paint in sealed compartments. *J. industr. Hyg.*, 1931. *13:* 333–337. [P]

1865. Dudley, S. F., F. G. Edmed, and R. C. Frederick. Further research on the production of carbon monoxide from paint in sealed compartments. *J. R. nav. med. Serv.*, 1933, *19:* 174-180. [P]

1866. Flagg, Paluel J. *The art of resuscitation.* New York, Reinhold Publishing Corporation, 1944, xv, 453 pp. [R]

1867. Gardner, H. A. The composition of paint vapors. *J. industr. Engng Chem.*, 1914, *6:* 91–95. [P]

1868. Giemsa, G. Irrespirable Luft in Schiffsräumen. *Arch. Schiffs- u. Tropenhyg.*, 1906, *10:* 143–158 [P]

1869. Giemsa, [ ]. Irrespirable Luft in Schiffsräumen. (Air irrespirable contenu dans certaines cales de navires). Abstr: *Hyg. gén. appl.*, 1906, *1:* 370–372.

1870. King, H. H. A study of vapors from drying paint films. *J. industr. Engng Chem.*, 1915, *7:* 502–504. [P]

1871. Klein, C. A. The composition of paint vapors. *J. industr. Engng Chem.*, 1915, *7:* 99–102. [P]

1872. Newington, F. H. The determination of carbon monoxide produced from painted surfaces in confined spaces. *J. Soc. chem. Ind., Lond.*, 1931, *50* (Transactions): 371T–375T. [P]

VIII. GAS EMBOLISM

Gas embolism may be defined as the propulsion of air or other gas in the circulation and its impaction in some portion of the vascular system. Although air embolism is of relatively infrequent occurrence in clinical medicine and surgery, the subject is of importance in relation to current theories of the cause of caisson disease and of escape "lung" accidents. Readers consulting the references which follow will also wish to refer to the sections on the physiology of decompression (p. 38), etiology of decompression sickness (p. 137), "lung" accidents (p. 223), and intravenous injection of oxygen (p. 288).

In 1864, Roger, quoted by Heuer, Andrus, and Taylor (*1884*) 1941, described a case in which collapse and clonic convulsions followed irrigation of a chronic empyemic cavity. A similar case was reported by Besnier (*1874*) in

1876. In 1876, Picard (*1888*) reported that injection of air into the portal vein of dogs results in death within 2 to 4 hours. The temperature fell during the period of coma preceding death and there was a fall in blood sugar and blood fibrin. Walcher (*1891*) 1876 described paralysis lasting 2 days in a case similar to those described by Besnier (*1874*) and Roger (see *1884*).

Brandes (*1875*) 1912 called attention to a patient who died in convulsions after injection of bismuth through a sinus into an empyemic cavity. At autopsy, there was bismuth in the smallest vessels of the cerebral cortex and with serial sections it was possible to trace the bismuth from the walls of the sinus up to the pulmonary capillaries and veins. Following this, there were several reports of convulsions, some fatal, following insertion of a needle for the induction of a pneumothorax or local anesthesia. These accidents were explained on the basis of air emboli introduced into the pulmonary veins and distributed into the arterial circulation with particular involvement of the cerebral hemispheres.

Heuer, Andrus, and Taylor (*1884*) 1941 gave the following typical clinical picture of cerebral air embolism: The patient becomes suddenly pale and there are patches of cyanosis on the skin. He may complain of pain in the chest on the side of the puncture with dizziness and spots before the eyes. The patient loses consciousness suddenly, the pulse is feeble, and there is stertorous respiration. The pupils are usually fixed and widely dilated, and there is sometimes strabismus. In the majority of cases, tonic or clonic convulsions occur, commencing in the external eye muscles or in the upper extremity and often becoming generalized over the entire body. The patient may die; in those cases which recover, the patient may be left with residual paralysis or visual disturbances for some time. There may also be persisting areas of paresthesia.

In addition to clinical observations upon the effects of spontaneous or accidental entry of air into the circulation, a number of experimental studies of the effects of air embolism deliberately produced in animals have been carried out. For such an early study, the reader is recommended to consult a thesis by Maguin (*1885*) published in 1879. A good historical review of the question of air embolism is provided in an inaugural dissertation published in 1906 by Bayer (*1873*). This author referred to death from air embolism following operations on the neck in which there was paralysis of the left extremities on the second day after operation, sudden fever and death on the fifth day. Foamy blood was found in the chambers of the heart. The author believed that veins in which there was a negative pressure were particularly likely to permit entry of air. Air injected experimentally into the left ventricle caused dilatation of the heart leading to death. Air bubbles were found circulating throughout the entire vascular system.

Couty (*1877*) 1877 found that injection of air into the aorta caused immediate death. Injecting air into the veins was less rapidly fatal, the animals succumbing in 5 to 10 minutes. The cause of death was stated to be the accumulation of air in the right heart and also obstruction by air bubbles of the flow of blood to the vital centers of the brain.

Pfanner (*1887*) 1936 raised the question of the effect of excess intrapulmonary pressure in the production of air embolism. He pointed out that air may get into the heart not only by accidental traumatic penetration of the lung but also by raised pressure in the lungs resulting from the passage of air under pressure into the respiratory system. Conditions in which expiration is hindered while inhalation is normal account for such excess intrapulmonary pressures and may be a cause of air embolism. Excessive pressure in the lungs may be developed during tetanic or epileptic seizures, and Pfanner believed it possible that cerebral air embolism may follow such attacks. As will be seen in the discussion on escape "lung" accidents (p. 223), intrapulmonary pressure may be greatly increased during ascent if the breath is held and this may lead to entry of air into the pulmonary circulation and death from air embolism.

Two recent experimental studies of gas embolism may be consulted. The first is a report by Curtillet and Curtillet (*1878*) 1939–40. These investigators injected air into the ves-

sels of frogs and rabbits, and subsequently examined the course of the air bubbles through the circulation with the microscope. In the frog, the air was resorbed in arterioles of 40μ to 50μ diameter. There was local arrest of circulation until the bubbles were absorbed, but no generalized interference with circulation. In dogs, air was injected into the carotid artery and it was found that the air bubbles were stopped by arterioles 30μ to 40μ in diameter. Moore and Braselton (*1886*) 1940 found that injection of air in a volume equal to or exceeding 0.5 cc. per lb. of body weight caused typical coronary death. Air was injected directly into the pulmonary vein of cats. In only a few cases was there any accompanying evidence of cerebral or medullary disturbances. It was found that injection of pure carbon dioxide into the pulmonary vein gave rise to no stable coronary embolus. Even with injections of 2 cc. of carbon dioxide per lb. of body weight, the gas was entirely taken up by the blood in 15 to 20 seconds and the heart was not visibly affected. Quite clearly, oxygen or carbon dioxide gas, experimentally introduced into the circulation, is much more readily dissipated in the body than air with its high inert nitrogen content. The danger of air injection is, therefore, much greater than oxygen or carbon dioxide injection.

1873. Bayer, Rudolf. *Zur Frage der Luftembolie.* Inaug.-Diss. (Med.) Freiburg, Speyer & Kaerner, 1906, 41 pp. [R]

1874. Besnier, E. Note sur un cas de mort subite par syncope survenue pendant l'operation de la thoracentèse et remarques sur la pleurésie gangréneuse primitive. *Bull. Soc. med. Hôp. Paris.*, 1876, *12:* 24–32 (memoirs). [P]

1875. Brandes, M. Ein Todesfall durch Embolie nach Injektion von Wismuthsalbe (Beck) in eine Empyemfistel. *Münch. med. Wschr.*, 1912, *59:* 2392–2394. [Ch]

1876. Brauer, L. Die Behandlung der einseitigen Lungenphthisis mit künstlichen Pneumothorax. *Münch. med. Wschr.*, 1906, *53:* 338–339. [P]

1877. Couty, [ ]. Expériences sur les effets des gaz artériels généralisés. *Gaz. hebd. Méd. Chir.*, 1877, *14:* 720. [P]

1878. Curtillet, E. and A. Curtillet. Étude expérimentale de l'embolie gazeuse. *J. Physiol. Path. gén.*, 1939–40, *37:* 573–584. [P]

1879. Doan, C. A. The capillaries of the bone marrow of the adult pigeon. *Johns Hopk. Hosp. Bull.*, 1922, *33:* 222–226.

1880. Dorello, F. and P. Rowinski. Sull'embolia da ossigeno puro. *Arch. Fisiol.*, 1938–39, *38:* 398–403.

1881. Fine, J. and J. Fischmann. An experimental study of the treatment of air embolism. *New Engl. J. Med.*, 1940, *223:* 1054–1057.

1882. Forlanini, C. Die Behandlung der Lungenschwindsucht mit dem künstlichen Pneumothorax. *Ergebn. inn. Med. Kinderheilk.*, 1912, *9:* 621–755 [P]

1883. Hamilton, C. E. and E. Rothstein. Air embolism. *J. Amer. med. Ass.*, 1935, *104:* 2226–2230. [Ch]

1884. Heuer, G. J., W. D. Andrus, and A. Taylor. Surgery of the thorax. *Nelson Loose-leaf Surgery*, 1941, *4* (chap. 5), 387–588. [R]

1885. Maguin, Albert. *Étude expérimentale sur l'introduction forcée et sur l'entrée spontanée de l'air dans les veines.* Thèse (Méd.) Nancy, Imprimerie Nancéienne, 1879, 47 pp. (P, R]

1886. Moore, R. M. and C. W. Braselton, Jr. Injections of air and of carbon dioxide into a pulmonary vein. *Ann. Surg., 1940, 112:* 212–218. [P]

1887. Pfanner, W. Ueber den intrapulmonalen Ueberdruck und die Ueberdruckluftembolie. *Münch. med. Wschr.*, 1936, *83:* 1266–1269. [R]

1888. Picard, P. Sur les injections d'air dans la veine-forte. *C. R. Soc. Biol. Paris*, 1876, Sér. 6, 3: 251–254. [P]

1889. Schlaepfer, K. Air embolism following various diagnostic or therapeutic procedures in diseases of the pleura and the lung. *Johns Hopk. Hosp. Bull.*, 1922, *33:* 321–330. [Ch]

1890. Van Allen, C. M., L. S. Hrdina, and J. Clark. Air embolism from the pulmonary vein. A clinical and experimental study. *Arch. Surg., Chicago*, 1929, *19:* 567–599. [P]

1891. Walcher, [ ]. Un cas d'empyème. *Gaz. méd. Strasbourg*, 1876, *35:* 1–5 [R, Ch]

1892. Weatherhead, E. Air embolism. *Brit. med. J.*, 1945, *2:* 333. [P, M]

IX. SUBMARINE ESCAPE "LUNG" ACCIDENTS

Development of the submarine escape "lung" and training of personnel in its use have provided an additional safety factor in the hazardous occupation of the submariner. For the literature on the "lung" itself, the reader will consult the section on the submarine escape "lung" (p. 255).

In trial escapes using the "lung," it was found that from time to time individuals suf-

fered from grave symptoms, sometimes fatal, which were different from typical caisson disease. These accidents were comparatively rare but their gravity made a careful investigation of them essential. In 1930, Polak and Tibbals (*1913*) reported such a fatal case following an escape from a stay of short duration at a depth of 30 ft. The victim had made two previous escapes with a "lung" from 7 and 15 ft. In the last escape, he ascended safely to a depth of 18 ft. from 30 ft. The ascent from 18 to 9 ft. was stated to have been made rapidly. He then continued slowly to the surface and collapsed after closing the valve of the "lung." He was recompressed to 20 lb. pressure and seemed to show some improvement. However, he soon collapsed again and died in spite of artificial respiration and other measures. At autopsy, the liver was found to be congested as were also the spleen and kidneys. The bronchi contained bloody mucus and air emboli were found in the heart, the coronary veins, and the veins of the pia mater. There were air bubbles in the visceral pleura as well. This case was diagnosed as one of caisson disease, in spite of the fact that the victim had been exposed to raised pressure for only 6 minutes. In view of the short exposure and shallow depth, there now is no doubt that the gas present in the circulation came from the lungs and was not liberated from solution in the blood and body fluids themselves.

In 1931, Adams (*1893*) called attention to the fact that the symptoms in "lung" training accidents appear within 1 to several minutes after reaching surface. At first, the men appear normal. Then follow abdominal cramps, dyspnea, headache, ocular pain, collapse, and unconsciousness. Oxygen and stimulants, according to the author, seem ineffective. A report was given in which recompression to 40 lb. pressure and subsequent slow decompression appeared to relieve the symptoms.

Brown (*1897*) in 1931 described three "lung" training accidents. In each case, there was dizziness, weakness, pallor, coldness of the skin, and collapse. All three victims were improved when recompressed to 30 to 45 lb. pressure and decompressed slowly. Brown believed that recompression probably should not have been tried since the symptoms were due to overdistention of the lungs and not to typical caisson disease. Subsequent experience proved that immediate recompression is the lifesaving measure in escape "lung" accidents.

After describing features of "lung" training, MacClatchie (*1911*) 1931 reported 3 cases of collapse out of 300 subjects who went through the training procedure. In 1 case, the accident occurred after an escape from the 50 ft. level. The victim did not stop at either the 20 ft. or 10 ft. level, and collapsed at the surface when the "lung" was removed. The pulse could not be felt at the wrist, the heart rate was slow, the body cold, and the muscles rigid. He was recompressed to 15 lb. pressure and recovered. In the second case, the escape was carried out from the 18 ft. level; the victim stopped at 10 ft. and then shot to the surface. He collapsed in a few minutes, but responded to warming and to stimulants. In the third case, the patient escaped from the 50 ft. level. Shooting to the surface from this level, he collapsed in 1 minute. The extremities were cold, the muscles rigid, and there was numbness in the right leg.Recompression failed to bring improvement, but the patient recovered spontaneously in 2 days. There was some question in this case as to whether the picture was not dominated by emotional factors.

Behnke (*1896*) 1932 stressed the importance of correct breathing in "lung" escape. It is essential that personnel avoid holding the breath, that the ascent be carried out at a regular rate, and that subjects have confidence in the "lung." Behnke reported one death from an escape at 15 ft., the victim having already made a safe escape from 7½ ft. He left the diving bell while reportedly breathing correctly, reached the surface, took off the "lung," and swam to the ladder, but collapsed before he could climb up. When pulled up, he was cyanotic, unconsciousness, and cold. There was hemorrhage from the nostrils. He died in a few minutes. At autopsy, there were hemorrhages in the lower lobes of both lungs. The right ventricle was dilated and the liver, kidneys, and spleen were congested. Subarachnoid hemorrhages were seen on the superior

precentral areas of the cerebral hemispheres. Increased intrathoracic pressure was given as the probable cause of accidents in "lung" escapes. It was considered that the cause of death was entrance of air into the general circulation either through the stomata of the alveolar walls or through rupture of the pulmonary vessels. Actually, gas bubbles have been found in the circulatory system in fatal cases. Several cases were reported in which recompression in the pressure chamber was helpful in the treatment of "lung" casualties.

Polak and Adams (*1912*) 1932 reported 10 accidents, 2 of which were fatal, in personnel undergoing the "lung" training. Nine of the cases were concerned with escapes from less than 30 ft. after short exposures to pressure. The authors stated that if the breath is held during escape, expansion of gas in the lungs may cause serious damage. In experiments on dogs to discover the mechanism of this damage, Polak and Adams found that an increase in intrapulmonic pressure resulted in a fall in systemic blood pressure and a rise in venous pressure. The right ventricle receives much less blood than normally. The authors believed that there was no question of heart failure due to rise in pulmonary blood pressure. In animals, it was found that an increase in intrapulmonic pressure to 80 mm. Hg, with a sudden release 10 seconds later, resulted in the presence of bubbles in the carotid artery. When the intrapulmonic pressure was raised to 100 mm. Hg, many bubbles appeared in the vascular system. The animals ceased to breathe although the heart continued to beat for approximately 2 minutes. At autopsy, interstitial emphysema was found throughout the mediastinum, and there were hemorrhages in the substance of the lungs. If pressure was applied in the lungs while the trunk was swathed in a tight bandage, no bubbles were present on release of pressure. However, when the bandage was removed and pressure again applied and released, bubbles did appear. In the dogs not protected by the bandage, the air embolism was due to raised intrapulmonic pressure plus stretching of the lung structure. Conscious human subjects can successfully exert pressures as high as 300 mm. Hg because of the resistance offered by tensed respiratory muscles.

It was found that recompression yielded good results in dogs, and it was stated that recompression should be carried out with the animal in the head-down position with the feet up. Adrenalin was given intravenously and in case of cessation of respiration, it was recommended that oxygen with carbon dioxide be administered.

Adams and Polak (*1894*) 1933 subjected dogs to the escape procedures in the escape tower, the first from the 50 ft. level. The animal rose to the suface in 12 seconds, exhaling all the way. There was no apparent distress nor any after effects. In the second escape, the animal was put out at the 85 ft. level and the ascent occupied 40 seconds. The animal exhaled during the last 20 ft. On reaching the top, the dog coughed and vomited about a pint of bloody liquid. There was dyspnea and weakness. The animal was killed and autopsied 1 hour later. Numerous hemorrhagic areas were found in the lungs, but no emboli. The lungs were filled with a frothy fluid.

Shilling (*1916*) 1933 studied the expiratory force of 419 men going through the training in the use of the "lung." The average expiratory force in the subjects was 114 mm. Hg. There was no correlation between the expiratory force and age, height, weight, and vital capacity. Three men lost consciousness trying to exert great force and several complained of dizziness. It was considered that the failure of some trainees to use the "lung" properly might be due to low expiratory force with consequent inability to exhale properly against the "lung" pressure. Subsequent improvements in the "lung" reduce the expiratory resistance and tend to obviate the danger from this cause.

Shilling and Hawkins (*1917*) 1936 reported on 2,143 simulated escapes in a pressurized diving tank made with the "lung" at 100, 150, 167, 185, and 200 ft. It was found safe under these conditions to remain at a simulated depth of 100 ft. for 37 minutes, at 150 ft. for 18 minutes, at 167 ft. for 17

minutes, at 185 ft. for 14 minutes, and at 200 ft. for 13 minutes. The subjects surfaced at a rate of 50 ft. per minute. It was found that air could be used safely in place of oxygen to charge the "lung" in escaping to the surface from depths of 100 and 150 ft. at a continuous ascent rate of 50 ft. per minute. Actual ascents were made without accident from 100 ft. after an exposure of 32 minutes and from 150 ft. after an exposure of 20 minutes.

In 1944, Gouze (*1905*) reported a case of air embolism in a diver in which the conditions appear to have resembled the accidents occurring to personnel making "lung" escapes. The diver in question descended to 40 ft., then ascended to 15 ft. and at this point fell to the bottom. At autopsy, air emboli were found in the heart and the vessels of the whole body and there were infarcts in the lungs, spleen, kidneys, and other organs. It was considered that the victim probably held his breath while coming to the surface and that expansion of air in the lungs resulted in rupture of lung tissue and entry of air into the vascular system.

A number of reports are to be found in the literature dealing with the effects of increased intrapulmonic pressure upon body function and upon the entry of air from the lungs into other tissues of the body. Some of these reports are included because it is considered that they will be of use to readers desiring to investigate further the mechanism of "lung" escape accidents. One of the earliest such reports is that of Ewald and Kobert (*1902*) published in 1883. In Ewald and Kobert's experiments, curarized dogs were made to breathe air at increased pressure. When the animals were killed and autopsied, air was always found in the heart but no lung lesions were ever observed. Observations were also made on rabbits and it was found that less pressure was required in these animals. Excised lungs tested under water at a low intrapulmonic pressure were found to be airtight. At high pressures, air passed through the uninjured walls of the lungs. In excised lungs of dogs and rabbits, a pressure of 35 mm. Hg was necessary to force air through the walls. Living dogs were able to withstand intrapulmonic pressures of 50 to 90 mm. Hg. The excised lungs of rats and guinea pigs leaked air when subjected to a pressure of 20 mm. Hg.

Katz (*1908*) 1908–9 found in experiments on rabbits that an intrapulmonary pressure of 20 mm. Hg was fatal, as was also a negative pressure of 20 mm. Hg. A positive pressure of 40 mm. Hg within the lungs could be endured if the abdominal cavity were filled with compressed air. In a report published in 1908–9, Rode (*1914*) found that in rabbits, intrapulmonary pressures of 38 to 39 mm. Hg resulted in penetration of air into the abdominal cavity. It was considered that air passed into the peritoneal cavity through a "sheath" around the pharnyx which is connected to the lungs at about the level of the sixth dorsal vertebra and which penetrates the diaphragm. Aerial communication between the cavities of the thorax and the abdomen was also considered in 1908–9 by Kronecker (*1909*).

The effect of raised intrapulmonary pressure on the circulation in the lungs was investigated by Cloetta (*1900*) in 1911. After a review of previous investigations, the author reported a fall of pressure in the carotid artery and rise of diastolic pressure in the right ventricle during expansion of the lung due to excess pressure. Chillingworth and Hopkins (*1898*) 1918–19 found that the carotid blood pressure fell during lung distention and that the respiratory rate was diminished. In 1920, Chillingworth and Hopkins (*1899*) found that in dogs very slight distention of the lungs caused a small rise in arterial blood pressure. With a greater distention, there was a marked fall in blood pressure. With a sufficiently great distention, the blood pressure fell almost to zero. It was stated that the lumen of the capillaries in the lungs may be reduced sufficiently to cause a rise in pressure in the pulmonary artery enough to distend the right heart. The fall in arterial blood pressure was ascribed to increased pressure on small pulmonary vessels, leading to a failure in supply of blood to the left heart. The degree of pressure required to occlude vessels may be re-

garded as an index of the pressure in the pulmonary arteries. According to the authors, this may reach 85 mm. Hg. Hopkins and Chillingworth (*1906*) 1920 found that when the lungs were artificially distended, the pulmonary arterial pressure tended to become equal to the systemic arterial pressure. Distention of the lungs to this point was found to be almost immediately fatal in dogs.

Experiments by Johnson and Luckhardt (*1907*) 1927–28 showed a fall in blood pressure as a result of raised intrapulmonary pressure. If maintained for a sufficient length of time, there was dizziness and unconsciousness in human subjects. After-effects included an increase in arterial blood pressure above normal, nausea, pounding in the head, discomfort, and a diminution in the knee jerks.

The effects of changes in intrapulmonary pressure on the pulmonary and aortic circulation of the dog were also reported by Sharpey-Schafer and Bain (*1915*) in 1932. Barach and Swenson (*1895*) 1939 found that breathing gases under positive pressures of 5 to 8 cm. H_2O resulted in an increase of 1 to 2 mm. in the diameter of the lumens of small and medium-sized bronchi during expiration. There were no definite effects during inspiration.

1893. Adams, B. H. Observations on submarine "lung" training. *Nav. med. Bull., Wash.*, 1931, *29:* 370–372. [R]

1894. Adams, B. H. and I. B. Polak. Traumatic lung lesions produced in dogs by simulating submarine escape. *Nav. med. Bull., Wash.*, 1933, *31:* 18–20. [P]

1895. Barach, A. L. and P. Swenson. Effect of breathing gases under positive pressure on lumens of small and medium-sized bronchi. *Arch. intern. Med.*. 1939, *63:* 946–948 [P]

1896. Behnke, A. R. Analysis of accidents occurring in training with the submarine "lung". *Nav. med. Bull., Wash.*, 1932, *30:* 177–185. [R]

1897. Brown, E. W. Shock due to excessive distension of the lungs during training with escape apparatus. *Nav. med. Bull., Wash.*, 1931, *29:* 366–370. [R, Ch]

1898. Chillingworth, F. P. and R. Hopkins. Physiologic changes produced by variations in lung distention. A body plethysmograph and its application to the study of lung distention in relation to circulatory phenomena. *J. Lab. clin. Med.*, 1918–19, *4:* 555–563. [P]

1899. Chillingworth, F. P. and R. Hopkins. Physiologic changes produced by variations in lung distention. II. Efficiency of the pulmonary circulation in overcoming obstruction. *Amer. J. Physiol.*, 1920, *51:* 289–302. [P]

1900. Cloetta, M. Über die Zirkulation in der Lunge und deren Beeinflussung durch Über- und Unterdruck. *Arch. exp. Path. Pharmak.*, 1911, *66:* 409–464. [P]

1901. Eisenmenger, R. Supraabdominale Saug- und Druckluftwirkungen und deren praktische Anwendung. *Wien. klin. Wschr.*, 1932, *45:* 1105–1108. [P]

1902. Ewald, J. R. and R. Kobert. Ist die Lunge luftdicht? *Pflüg. Arch. ges. Physiol.*, 1883, *31:* 160–186. [P]

1903. Frumina, R. Über die Störung des Lungenkreislaufes unter dem Einflusse verminderten oder vermehrten Luftdruckes. *Z. Biol.*, 1908-09, *52:* 1–15. [P]

1904. Gonzalez Gil, U. Accidentes respiratorios en el deporte de la "caza submarina". *Sem. méd. expañ.*, 1944, *7:* 148–152.

1905. Gouze, F. J. Air embolism in a diver. Report of fatal case. *Nav. med. Bull., Wash.*, 1944, *43:* 538–542. [Ch]

1906. Hopkins, R. and F. P. Chillingworth. Physiologic changes produced by variations in lung distention. III. Impairment of the coronary circulation of the right ventricle. *Amer. J. Physiol.*, 1920, *53:* 283–292. [P]

1907. Johnson, C. A. and A. B. Luckhardt. Studies on the knee jerk. III. The effect of raised intrapulmonic pressure upon the knee jerk, arterial blood pressure and the state of consciousness. *Amer. J. Physiol.*, 1927–28, *83:* 642–652. [P]

1908. Katz, S. Die Atmung bei verändertem intra- und extra-pulmonalem Drucke. *Z. Biol.*, 1908–09, *52:* 236–250. [P]

1909. Kronecker, H. Aerial communication between the cavities of the chest and the abdomen. *J. Physiol.*, 1908–09, *38:* lxxvP. [P]

1910. Liebig, G. von. Ueber die Blutcirculation in den Lungen und ihre Beziehungen zum Luftdruck. *Dtsch. Arch. klin. Med.*, 1872, *10:* 234–254. [P]

1911. MacClatchie, L. K. Medical aspects of submarine "lung" training. *Nav. med. Bull., Wash.*, 1931, *29:* 357–366. [R, Ch]

1912. Polak, B. and H. Adams. Traumatic air embolism in submarine escape training. *Nav. med. Bull., Wash.*, 1932, *30:* 165–177. [R]

1913. Polak, I. B. and C. L. Tibbals. A fatal case of caisson disease following a dive of short duration to a depth of thirty feet. *Nav. med. Bull., Wash.*, 1930, *28:* 862–865. [Ch]

1914. Rode, R. Die Luftbahn zwischen Brust- und Bauchhöhle. *Z. Biol.*, 1908–09, *52:* 415–429. [P]

1915. Sharpey-Schafer, E. and W. A. Bain. The effects of changes in intrapulmonary air-pressure on the pulmonary and aortic circulation of the dog. *Quart. J. exp. Physiol.*, 1932, *22:* 101–147. [P]

1916. Shilling, C. W. Expiratory force as related to submarine escape training. *Nav. med. Bull., Wash.*, 1933, *31:* 1–7. [P]

1917. Shilling, C. W. and J. A. Hawkins. The hazard of caisson disease in individual submarine escape. *Nav. med. Bull., Wash.*, 1936, *34:* 47–52. [P]

X. "BLOWING UP"

Under certain conditions, divers have been forced rapidly to the surface because of filling of their diving dress with air. These accidents result in acute manifestations of caisson disease and are properly discussed under that subject. However, they are referred to separately here because of the somewhat special problems they raise.

von Wenusch (*1918*) 1896 described the case of a diver who lost his life through too rapid surfacing. This diver surfaced rapidly from a depth of 35 m. of water. He collapsed and died almost immediately, artificial respiration being of no avail. At autopsy, the face and front of the body were rigid, the conjunctivae injected, and the pupils dilated. There were punctate hemorrhages in the brain and gas bubbles were found in arteries, veins, and capillaries throughout the body. The heart was dilated and foamy blood was present in all chambers. Large gas bubbles were seen in the portal veins and inferior vena cava. The spleen was enlarged, the kidneys hyperemic, and the liver hemorrhagic.

1918. Wenusch, F. R. von. Ueber einen Fall von Tauchertod. *Wien. klin. Wschr.*, 1896, *9:* 774–776. [Ch

XI. DIVER'S "SQUEEZE"

As the diver descends into the water, the air pressure within the helmet and suit must be increased with the increasing pressure of the column of water against the surface of the body. Should the pressure within the helmet suddenly fall, or if the hydraulic pressure on the outside of the body were to increase without a corresponding increase in the air pressure within the helmet, the differential of pressure thus created would interfere with respiration, and drive blood into the head and neck or even force the body itself up into the helmet. This so-called diver's 'squeeze" occurs if a diver on the bottom falls off a ledge to a new lower level without a corresponding increase in helmet pressure.

What appears to be the first reported case of diver's "squeeze" was described in 1842 by Liddell (*1922*). The victim was a diver of 26 years of age working at a depth of 80 ft. While he was engaged in his work, the airline burst above the water. The attendant closed the hole with his hand and pulled the diver rapidly to the surface within a minute and a half after the accident. Blood was streaming from the ears, nose, and mouth and the face and neck were swollen and discolored. The patient was still conscious. He was taken to the hospital within 1 hour and there it was discovered that he had dark patches of ecchymosis on the neck and shoulders. No such spots were seen below the helmet line. The mucosa of the cheeks, tongue, pharynx, and tonsils were black and engorged. The conjunctivae were engorged and inflamed. The patient continued to vomit blood but by the next day, the swelling and lividity began to subside. He complained of headache and faulty vision. He was treated symptomatically and gradually all symptoms and signs disappeared.

A similar accident was reported a year previously in which there was some bleeding and discoloration of the skin. The ecchymosis disappeared within a month and the diver resumed his work. The author also reported an accident to the air tube of a diving bell. One of the occupants was caught underneath the bell and had difficulty extricating himself. His body was blackened with ecchymosis down to the waist. The symptoms in the cases described were recognized by Liddell as being caused by a sudden lowering of air pressure within the helmet, air continuing to escape from the helmet by way of the escape valve. Since the body was no longer protected by the inflated suit, the hydraulic pressure outside the body forced blood into the head and neck. The author suggested equipping divers with a valve in the junction of the airline and suit which would allow air to enter the suit but not to escape in case of sudden failure of the airline.

A case of diver's "squeeze" was described in 1931 by Caputi (*1921*); in 1943, Sala and Shaw (*1923*) reported two cases neither of

which was fatal. The first victim had worked for 17 minutes at 35 ft. when the lifeline became fouled in an anchor chain and he was unable to signal to the surface crew. When he did not answer the signals, he was brought to the surface unconscious. Soon, however, he regained consciousness and complained of severe headache. There was bleeding from the nose, mouth, and ears and purple discoloration of the skin of the scalp, face, neck, chest, and back. Petechial hemorrhages were present in the conjunctivae and mucosa of the soft palate and nasopharynx. The middle ears were full of blood. There were tremors of the upper extremities but no paralysis. The patient complained of pain in the right side of the chest. Oxygen was administered and the patient was gradually relieved. The second victim was injured while descending to a depth of 36 ft. He began to lose consciousness and signalled to be pulled up. At the surface, he complained of severe headache and there was cyanosis of the head, face, and neck with subconjunctival hemorrhages. There was bleeding from the nose and the middle ears contained blood. There was frequent vomiting of blood and mucus. The patient has treated with oxygen. The areas of subconjunctival hemorrhage persisted for 10 days and the patient recovered completely within a month. The symptoms in both of these cases were ascribed to a negative pressure differential within the helmet, driving blood from the abdomen and lower extremities into the thorax, head, and neck.

Relatively small pressure differentials are sufficient to halt respiration. Davis (*48*) 1934 called attention to an early device for breathing under water in which the subject was supposed to breathe through a tube running from the mouth to the surface of the water. Under such conditions, the intrathoracic pressure would be that of the atmosphere while the pressure outside the thorax would equal the atmospheric pressure plus the weight of the column of water at the depth to which the diver was exposed. Such a device is completely impractical. Stigler (*1924*) 1911 experimented with tolerance of such pressure differentials and found the maximum depth at which respiration could be carried out was 192 to 200 cm. Stigler withstood differential pressure at a depth of 600 cm. (from breast to surface) for 3 to 4 minutes. He tolerated 2 m. for 18 seconds. After this experiment, he was forced to remain in bed for 7 weeks and was left with persistent cardiac damage. Stigler (*1924*) 1911 reported that raised extrathoracic pressures in excess of the intrathoracic pressure caused restriction of respiration and circulation and congestion of the blood in the thoracic organs. A pressure differential corresponding to 2 m. of water, according to the author, could kill a man in 1 minute.

Referring to diver's "squeeze," Bornstein (*1919*) 1918 described symptoms arising from nonfatal pressure differentials. There is loss of breath as if the sternum had been pressed in; respiration is accelerated, and there is a feeling of pressure in the head and the sensation of the eyes popping out of the head. Usually, these symptoms vanish rapidly. Carrying out experiments in a diving tank, Bornstein breathed air at a differential of 50 mm. Hg which he was able to support for only 20 seconds. In 1919, Bornstein (*1920*) referred to experiments on dogs in which breathing air at pressure differentials simulating those occurring in diver's "squeeze" caused dilatation of the right heart, bloody extravasation into the lungs, and marked congestion in the liver and kidneys. Bornstein understood the mechanism of diver's "squeeze" and recommended modifications of the helmet to prevent the condition.

Wiethold (*1926*) 1936 referred to cases of "squeeze" among granite and stone fishers who dive in rigid helmets. In such victims, the face and head were congested. There was bleeding from the nose, and the tongue was swollen and blue-violet. There were petechial hemorrhages in the buccal mucosa and the nose and ears were filled with blood. In fatal cases, the brain and meninges were hyperemic and small hemorrhages were observed in the vessels of the pons. The lungs were hyperemic, the bronchioles being filled with mucus and blood.

Wiethold (*1926*) 1936 cited the case of a diver who had worked for 35 minutes at 30

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m. and who fell from this position to a lower level. At autopsy, the head was bloated and the soft parts were blue and congested. There was intense hyperemia of the brain and meninges and congestion of the bronchial mucosa. Wiethold stated that personnel who fall after having worked for a long period on the bottom suffer more severe effects than those who have not. He thought decompression might be a factor in "squeeze". When a diver falls, he is pulled rapidly to the surface and there is danger of air emboli, especially since the alveoli probably contain edema fluid and blood and elimination of gases may be interfered with. If it is true that rapid decompression may be a contributory cause of death, treatment, according to Wiethold, must consist in recompression to the pressure at which the victim was working. Wiethold believed that only in falls occurring at the beginning of work should immediate decompression without therapeutic recompression be allowed.

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XII. UNDERWATER BLAST

Following disasters at sea, submarine personnel may be exposed to injury by underwater blast. In particular, divers operating in mine-infested waters or clearing harbors of wreckage left by the enemy may be exposed to submarine explosions. For this reason, the subject of blast injuries is of concern to medical officers responsible for the care and protection of submarine crews and divers.

Many of the advances in our knowledge of the pathology, treatment, and prevention of underwater blast injury have been set forth in unpublished classified reports. Much of the significant work has been carried out by research investigators attached to naval diving activities, making use of experimental conditions simulating the environment of the diver. The open literature, however, contains a number of significant reports and these will be briefly analyzed.

For information on the effects of air blast, the reader is recommended to consult reports by Hooker (*1942*) 1923–24 and Blalock and Duncan (*1927*) 1942. Reference should be made to a review on blast and concussion published in 1942 by Fulton (*1935*).

In 1917, Mathew (*1943*) described the effects of a submarine mine explosion in which the men nearest the mine, that is to say, those almost immediately above it, were blown straight upward out of the water and were uninjured. Those further away received the force of the explosion through the water. There were 10 cases of injury, all of whom reported hemorrhage from the nose and ears at the time of explosion. There was abdominal tenderness, blood in the urine and feces, and all had a sense of constriction in the chest. Seven recovered in 4 days while 3 required longer hospitalization.

Ratelier, Le Berre, and Lomas (*1950*) 1918 described three cases of peritonitis following tears in the intestine. In one case, there was a rupture in the transverse colon in a patient who died 3 days after underwater blast injury. In a second patient who died 2 days after being exposed in the water to a depth charge, there were two perforations along the free border of the ileum near the cecum. The rupture probably occurred at the moment of the explosion. In a third case, the patient suffered from general peritonitis following underwater explosion of a mine. At operation, a perforation of 9 mm. in diameter was found on the free border of the jejunum. The perforation was sutured, drainage instituted, and the patient recovered.

An experimental study of the pathological changes produced by depth charges was carried out upon animals by Cameron, Short, and Wakeley (*1929*) 1942–43. Animals were fastened at fixed points in relation to a 320 lb. charge of TNT suspended at a depth of 48 ft. in water 90 ft. deep. The animals exposed to the explosion of this charge developed pulmonary hemorrhage, interstitial emphysema, and sometimes hemorrhage and tearing of the walls of the alimentary canal. Occasionally, there was hemorrhage in the pericardium, spleen, kidneys, and ductless glands. The most severe injuries were seen in those animals stationed within a 40-yard radius of the charge. Eleven of the thirteen of these animals were killed instantaneously. Hemorrhage developed in animals as far as 100 yards away. Hemorrhage affected the right lung more frequently than the left and clots were seen in the bronchi. It was found that acute pulmonary hemorrhage might occur without immediate death or that animals might be found dead without extensive pulmonary lesions. Acute vesicular and interstitial emphysema was practically a constant finding in all animals within a radius of 40 yards. The upper lobes were most frequently affected. Sometimes there was a pneumothorax or a hemothorax. Very little damage to the soft structures of the body, the bones, gall bladder, the urinary bladder, or the body wall was seen.

For detailed studies of immersion blast injuries, the reader is referred to a series of articles appearing in volume *41* of the *U. S. Naval Medical Bulletin* (1943). In the first of these, McMullin (*1944*) 1943 pointed out that the principal damage in underwater blast is to the lungs and to the walls of certain loops of intestine. There may be rupture of intestinal vessels leading to hematomata and paralytic ileus, or there may be perforation of the intestine with generalized peritonitis, abscess formation, or intestinal gangrene. No injuries to the liver, spleen, stomach, or kidneys were observed. McMullin rejected the theory that blast injuries are caused by water forced up the rectum. He considered that blast injuries might be eliminated or minimized by wearing protection on the chest and abdomen and by instructing men to swim on the back when exposed to the hazard of underwater explosions. Regarding treatment, the author believed that this should be conservative in the majority of cases and should include counteracting shock, maintenance of fluid intake by transfusion, avoidance of medication or nourishment by mouth, administration of morphine for restlessness and pain, Wangensteen suction to reduce intraintestinal pressure, intravenous administration of sulfa drugs, and administration of oxygen. Surgical intervention should not be undertaken except for specific indications. McMullin considered that operation was contraindicated if the patient was first seen several days after the accident and was suffering from general peritonitis. Recent perforation demands surgical intervention. Where surgery was attempted, the simplest operation was considered the safest for blast cases. These patients are poor operative risks at best.

Palma and Uldall (*1946*) 1943 stated that immersion blast injury is chiefly characterized by abdominal pathology, with secondary effects in the lungs and in the central nervous system. External injuries were not found. Thirty-five cases were seen in hospital 5 days after injury. Sixteen were ambulatory with few complaints. Some of these showed X-ray evidence of blast injury in the lungs. In 14 patients, there were severe abdominal injuries and of these, 8 recovered without operative interference, 2 recovered with operation, and 4 died. In 4 patients, the findings were comparable to those reported in atmospheric blast injury and in 1, there were transient psychological changes. Pugh (*1948*) 1943 reported 7 cases, 2 of which were fatal. One died 12 days after immersion blast injury with multiple perforations of the lower ileum and the jejunum, general peritonitis and contusions in the lungs. In the other fatal case, there were massive destruction of the cecum and ascending colon and lung contusions. The author reported an operation in which a gangrenous loop of jejunum 40 cm. in length was successfully removed and another case in which a fecal fistula developed as a sequel to an abscess in the upper right quadrant. A large portion of omentum sloughed away through the fistula

and the patient recovered. In a study of the radiological findings in immersion blast injuries, Gates (*1937*) 1943 found abnormal densities in one or both lungs in 30 cases (86 percent of the total). In the abdomen, there was some degree of gaseous distention in the small intestine in all cases seen. There was X-ray evidence of perforation in 4 cases. In two of these, free gas was present in the peritoneum and in the other two, small bubbles of gas were observed apparently in tissues outside the intestinal tract. Large, soft-tissue densities, presumably due to accumulation of fluid were seen in 4 cases. X-ray studies of the gastrointestinal tract with barium in 5 recovered cases revealed undoubted abnormality in the mucosal pattern of the walls of the small intestine in 1 case and a fecal fistula at the hepatic flexure in another.

According to Ecklund (*1932*) 1943, atmospheric blast injuries are characterized by the absence of external signs of trauma, extensive effusion of blood and fluid into the pleural spaces, and hemorrhage into the pulmonary tissue. In atmospheric blast injuries, the principal seat of trauma is in the thoracic cavity. In regard to immersion blast injuries, the author's cases showed predominant and most urgent pathology in the abdomen, although pulmonary lesions were also seen. Perforations of the small intestine near the ileocecal valve, as well as tears in the duodenum and the cecum were found. Microscopically, hemorrhages into the alveoli were observed, with lysis of the erythrocytes and liberation of iron pigments. In some cases, the lung structure was destroyed by massive hemorrhage. Intestinal perforations exhibited a "blown-out" character. There were extensive peritonitis and attempts at walling off the infection. There was notable absence of injury to the liver, spleen, kidneys, or bladder.

As Hamlin (*1941*) 1943 has stated, knowledge of the effect of immersion blast on the nervous system is somewhat scanty. In the author's cases, it was seen that the nervous system is vulnerable when exposed to underwater detonation. However, it was impossible to explain the exact mechanism and neuropathology of immersion blasts. Although the central nervous system is vulnerable, it is less so than the thorax or abdomen. Hamlin raised the possibility that paralytic ileus may be of central nervous origin. He thought that possibly the blast wave may be transmitted to the spinal cord and thence to the cranial cavity, setting up a convection force in a cephalad direction through the spinal fluid and possibly the neuraxis itself. Such a mechanism could conceivably damage the delicately supported vessels of the leptomeninges, leading to subarachnoid hemorrhage and neurological symptoms. Injury to the cortex and deeper centers was possible. The author suggested that temporary unconsciousness after the blast was probably caused by a shift in the vascular reservoirs of the great vessels resulting in transient cerebral ischemia.

The reader is referred to a significant experimental study of underwater concussion carried out by Greaves, Draeger, Brines, Shaver, and Corey (*1940*) and published in 1943. This report is based on data obtained on rats and guinea pigs exposed to explosions of *tetryl* in a steel tank containing fresh water. The charge was detonated 20 inches below the surface while the animals were swimming within a 2-ft. circle around a point directly over the charge. Goats were exposed to a 300-lb. depth charge exploded 50 ft. below the surface in water 100 ft. deep. The investigators pointed out that the *airborne* blast wave consists of a shell of compressed air moving outward from the explosion center. The cross section of the shell is a steep fronted wave followed by a negative or suction phase. The concussion wave *in water* has a velocity of 4,800 ft. per sec. (the rate of sound in water) and consists of the (a)-phase or concussion phase which is the destructive factor; the (b)-phase is the disturbance produced by the expanding bubbles of gas liberated by the explosion. This phase is not selectively destructive in water. The compression phase tends to reflect as a tension wave when it strikes another medium. This occurs when it reaches the surface of the water, but if its pressure is approximately 500 lb. per sq. in. or greater it breaks through into the air with a shredding effect and

literally "blows off" the surface. The determining factor in the production of injuries by blast is the presence of air or gas in the tissues. The authors' experiments confirm the susceptibility of gas-filled tissues to the effects of underwater blast. The lungs and intestinal tract and alimentary tract are especially susceptible. Injuries occur in the skull and upper respiratory passages when the head is submerged at the time of explosion. Pathological lesions are not seen in solid organs and in tissues that do not contain air or gas. It was suggested that the underwater concussion wave produces tissue injury by *shredding* the tissue as it passes from a solid into a gaseous medium within the body. The authors pointed out that kapok and foam rubber prevent or minimize the injurious effects of the compression wave.

The pressure to which the body will be exposed may be calculated from the formula, $p = 4{,}333 \dfrac{w^{1/3}}{r}$, where p = lb. per sq. in., w = weight of the charge, and r = range in yards. This formula applies in TNT and similar explosives. With this formula, the safe ranges for divers who may be subjected to underwater concussion can be determined, using 50 lb. for the value of p (Webster, unpublished communication).

Friedell and Ecklund (*1934*) 1943 carried out experiments on immersion blast injury in which they exposed guinea pigs to detonating charges consisting of detonating caps containing 35 grains of mercury fulminate. The guinea pigs were placed in a tank of water 6 by 8 ft. in diameter and 4 ft. deep. The detonating charge was set off electrically under the animal. Two types of lesion were found in the abdomen: (*a*) hemorrhages into the bowel wall and (*b*) intestinal perforations and tears. The lesions in the chest consisted of symmetrical areas of hemorrhages on that surface of the lungs nearest the explosive force (usually the dependent edges of the middle lobes on both sides). Thoracic involvement accounted for death in most animals, according to the authors. No abdominal lesion was found except when the thoracic damage was so severe as to cause death. Perforations of the alimentary tract occurred over areas containing scybalous fecal masses and probably over air bubbles. In immersion blast, perforations of the gut are the immediate result of the blast and not the subsequent results of necrosis of the bowel wall. They demand, therefore, early surgical intervention. Hemorrhagic lesions, however, do not require operative treatment. A rigid covering was shown to protect the thorax of animals exposed to immersion blast and the authors considered it reasonable to assume that extension of the life jacket to cover the abdomen would be beneficial. Theories of causation of immersion blast and air blast are still controversial.

In another paper in the symposium on immersion blast, Friedell and Burke (*1933*) 1943 advanced a theory to account for the more destructive effect of immersion blast than of air blast. This theory takes into account the *brisance* of an explosive, the elasticity of the medium, its density, and the factor of distance. Of the two types of lesions observed, the hemorrhagic type was considered to be the result of the percussive effect of the blast while the perforations of the intestines were thought to be the effects of the secondary blast pressure or the concussive effect.

Five cases of immersion blast injury occurring in 1942 were reported by Pinnock and Wood (*1947*) in 1943. After the torpedoing of the vessel in question, two depth charges exploded in quick succession. Patients stated that they felt as if they were kicked in the stomach or in the back of the pelvis. All were hospitalized within 4 hours. All four cases with gut injury died subsequently. In two of these, the clinical appearance was misleadingly good, but all had abdominal rigidity. It is significant that victims of immersion blast injury often look quite well although in grave condition. Boardlike rigidity of the abdominal wall should be regarded as evidence of gut perforation and not readily ascribed to other causes. Two unusual cases of water-blast injury were reported by Pugh and Jensen (*1949*) 1943. In the first case, there was perforation of the jejunum 2 ft. below the ligament of Treitz. This perforation sealed itself off spontaneously. However, the patient

developed volvulus of the jejunum, a rare sequel. In this particular case, the proximal portion of the jejunum was gangrenous for a distance of 40 cm. The volvulus was caused by adhesion of the bowel at the side of the jejunal perforation to the parietal peritoneum opposite the upper pole of the left kidney. The gangrenous bowel was resected and continuity reestablished in spite of great difficulty. The patient recovered. Pugh and Jensen (*1949*) recommend the lifesaving value of the Murphy button in establishing the anastomosis in this case. In the second case reported by Pugh and Jensen, the entire omentum sloughed off, as well as an 8 cm. segment of the hepatic flexure and the transverse colon. The bowel went on to reestablish its continuity spontaneously and recovery followed. Both cases developed intercurrent pneumonia from which they recovered.

Webster, Ross, and Alford (*1952*) 1943 described immersion blast injuries in 15 survivors of a torpedoed ship who had been subjected to the effect of an exploding depth charge while in the water. Many vomited and spat blood and developed pain when taken aboard the rescue vessel. The patients were in varying degrees of shock. On admission to the hospital, there were severe abdominal pain, vomiting, hematemesis, and bloody diarrhea. There was also some distention and rigidity of the abdominal wall. Four patients died on the first day of admission, 1 in the second, 1 on the fifth, and 1 after 6 weeks. In 4 cases, there was protracted convalescence, while 7 patients recovered rapidly within 3 to 14 days. The authors called attention to the almost complete absence of chest signs and symptoms. This may have been due to the fact that nearly all personnel wore kapok life preservers when they were thrown into the water. In some prolonged cases of convalescence, there may have been submucosal hemorrhages in the bowel wall which permitted infiltration of invading pathogenic organisms. In 2 such cases, sulfathiazole was apparently beneficial. The authors were of the opinion that submucosal and petechial hemorrhages in the wall of the intestine could interfere with the neuromuscular mechanism and cause paralytic ileus, and, if gross, even sloughing and perforation. They recommended that naval personnel be warned of the danger of immersion blast at sea and that they be advised to swim as quickly as possible away from the abandoned ship. It was considered advisable for personnel in the water to keep as much of the body out of the water as possible. Life preservers of kapok designed to cover the abdomen and chest were recommended. In treatment, the management of shock, including blood or plasma transfusion, was of primary urgency. These cases should be regarded as medical or surgical emergencies and treatment decided upon and instituted at once. Early chemotherapy should be considered.

The reader is advised to consult a report by Cameron, Short, and Wakeley (*1930*) 1943–44 containing a discussion of 20 cases of underwater blast which came to surgical operation. There was 1 case of rupture of the transverse colon, another case with perforations of the wall of the cecum, a case of rupture and injury to the duodenum, a case of retroperitoneal hemorrhage, a case with injury to the liver, a case with punched-out perforations of the ileum and a small perforation of the sigmoid colon with numerous subserous and retroperitoneal hemorrhages. The paper also contains a survey of 80 cases of immersion blast which recovered without operation. Experiments were carried out on goats and monkeys. Lung lesions were more severe and bronchial and tracheal clots more common in those goats in which the thorax as well as abdomen was immersed during the underwater explosion than when the abdomen alone was submerged. Bleeding *per rectum* and mesenteric hemorrhages were more marked when the abdomen alone was submerged. Intestinal lesions were common in these experiments. There were hemorrhages in the mucosa, perforations with bleeding into the lumen, and mesenteric hemorrhages. There was a striking similarity in the microscopical appearances of the lesions in all the experimental animals. The lesions were essentially mucosal in position, the outer layers of the gut wall not being affected except in cases of perforation. Hemorrhage, when present,

tended to show an annular distribution. No anatomical explanation for this is forthcoming. No regular association was found between the anatomical arrangements in the gut wall and the localization of the hemorrhage.

Gill and Hay (*1938*) 1943–44 described 16 clinical cases of abdominal injury due to underwater explosion. Six cases were operated upon and 4 of these died. Two of the remaining 10 died without operation, while the rest recovered. The authors have arranged their cases into 3 groups or types: In type I, there is severe shock which may be rapidly fatal. In this type, the patients suffer from a gross splanchnic insult, usually with rupture of the viscera and internal hemorrhages. Very little can be done for these cases. Type II is described as the "classical" type. In these cases, there is perforation of a hollow viscus at the time of injury and usually great surgical shock. In type III, the bowel is injured but not perforated. In only 3 cases described by the authors was there any involvement of the lungs and all of these patients died. In the abdomen, the viscera in the lower portions of the cavity were most commonly affected. Injuries were mainly located on the antimesenteric surface of the intestine. The authors discussed the possible mechanism of action of the blast wave in producing the injuries described.

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XIII. DROWNING

The danger of drowning in submariners, divers, and caisson and tunnel workers is probably greater than in other occupations. However, it has not been considered pertinent to include an extensive bibliography of the literature on death from submersion. Standard works on medicine and occupational diseases may be consulted. The reader may also care to refer to reports by the following authors: Beau (*1957*) 1860, Guillain (*1960*) 1931, Devix and Plauchu (*1958*) 1932, and Güttich (*1959*) 1939.

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XIV. PSYCHIATRIC DISTURBANCES

A careful search of the literature reveals very little written on the psychiatric problems of submarine personnel, divers, and caisson and tunnel workers. Submarine and diving personnel in the U. S. Navy have shown remarkably good psychological adjustment to the hazardous conditions under which they have had to operate. This is partly attributable to the care that has been taken in the selection and training of submarine and diving personnel and to the high level of morale which is traditional in these branches of the naval service. A significant factor also must be the rapid strides which have been made in improving the conditions of habitability in submarines, the development and application of new safety and rescue devices, periodic medical examination, attractive diet, and adequate rest periods in an interesting environment. The problems of duration of watches, length of war patrols, numbers of war patrols, and frequency and duration of rest periods need careful study in conjunction with new developments in submarines and predictable new conditions of service. New engineering developments will make possible greatly prolonged periods of continued submergence and it is highly desirable that carefully planned psychiatric research be conducted to investigate the effects of such conditions upon mental health of personnel, and that procedures be recommended which will minimize the likelihood of psychiatric breakdown.

Submarine crews under conditions of active service are so well adapted to their environment that many of the psychiatric problems which might be expected to arise are almost never encountered. Claustrophobia—the exaggerated fear of enclosed spaces—for example, does not ordinarily present a problem and submariners very early become adjusted to the restricted spaces in which they must work. However, a report of Benon (*1961*) 1936 of the psychiatric picture in a civilian making his first submarine trip (in France) illustrates a type of psychological disturbance which may flare up in ill-adjusted individuals or in persons not correctly indoctrinated. The patient described by Benon was a man 31 years of age. He went aboard a submarine as an observer at 1800 on the 19th of July, 1932. As stated, it was his first experience in a submarine and he was anxious for two reasons: In the first place, his wife was ill, and secondly, he was apprehensive because of a recent accident in which a submarine had gone to the bottom with the loss of more than 40 lives. He spoke

with anxiety of this tragedy and his morale was clearly low before coming aboard. On the evening of the 19th of July, he was distraught and did not reply to his comrades' questions. He wandered about looking to the right and to the left as if unsure of himself, but he was in no great agitation. On the 20th, diving operations were carried out from 0400 to 2000. At noon, he refused to eat. The maneuvers were carried out without any kind of mishap or unusual incident except that the crew were fatigued by heat and the carbon dioxide level was rather high. The submarine returned to its base about midnight. The next day, the patient did not appear at the submarine base, but fell into a state of partial mutism and stupor. He was taken on the 22nd to Nantes and kept there until the 12th of August. On the nights of the 22nd and 23rd of July, he was agitated and cried out that the "submarine was leaking." The state of partial mutism persisted for about 6 months. During this time, he did not refuse nourishment. There was gradual but progressive improvement and he was finally discharged in an asthenic state tending to chronicity. There was some amnesia for the whole experience in the submarine and he continued to complain of headaches, pains in the back, deafness, ringing in the ears, disturbances of vision, and insomnia. There was no family history of mental or nervous disease and he had previously a good record in his work.

Submariners may be exposed to the dangers of psychological and emotional upsets through living in cramped quarters even in the absence of the special dangers which are inseparable from war patrols. Given well-selected and trained personnel, a good commander can do much to maintain favorable morale under these conditions and submariners learn habits of consideration for one another which make life aboard the submarine much more tolerable. The problems arising out of acute anxiety during war patrols in enemy waters, particularly during depth-charge attacks require competent handling by all concerned. The morale of the men suffers during unsuccessful patrols and when it is necessary to endure the enemy's depth charges without being able to strike back. An excellent remedy for such tension is the successful destruction of an enemy target.

Much has been said of the beneficial effects of routine discipline in the maintenance of morale and the prevention of psychological disturbances in personnel. This applies particularly to the submarine crews. Although discipline is not obtrusive aboard a submarine and there may be a rather informal relationship between officers and men, a true condition of efficient discipline is at all times preserved and every man carries out his duties meticulously and takes personal responsibility for them.

In performance of routine duties, it is important that optimum hours of concentrated attention at any one task should be worked out. Will (*1962*) 1945 has discussed this problem in relation to operators of antisubmarine sound gear. He pointed out that monotonous, repetitious work requiring constant attention but infrequent intellectual efforts may give rise to nervous tension, anxiety, and fatigue. Two case histories were reported in which apparently well-adjusted individuals suffered mental breakdown attributed to overprolonged periods of duty under tension. Job analyses of submariners should from time to time be carried out and recommendations be made, on the basis of the best possible evidence available as to hours of watch, rest, sleep, and length of patrols. It should be remembered also that conditions of the air—low oxygen concentrations, high concentrations of carbon dioxide, and extremes of temperature and humidity—may in themselves produce psychological abnormalities. In particular, anoxia and high concentrations of carbon dioxide may result in mental sluggishness, delayed reaction time, and even definite psychiatric manifestations.

The psychological problems of deep sea divers show certain specific differences from those created by the environment of the submarine. The diver must accustom himself to the experience of being enclosed in the diving dress and having the helmet screwed down over the head. He must be lowered into the water to the bottom, where he carries out

hard manual work under conditions of cold and faulty illumination. Often, he must operate in mud and silt and he is constantly hampered by his suit and his gear. In addition, he must do his work alone without companionship of a nearby comrade with whom to talk. True, he is in communication with the surface crew on whose efficiency his life depends. Considering the special hazards which he must constantly face, it is surprising not that divers occasionally suffer from psychiatric disturbances, but that they remain so free of such abnormalities. Again, the remarkable performance of Navy divers in World War II must be attributed in part to the careful job of selection and training that has been carried out.

Certain specific psychological disturbances associated with diving are referred to elsewhere in this Sourcebook. The reader should consult references to slowed reaction time and mental sluggishness in deep diving in the literature on the mental effects of nitrogen narcosis (p. 162). As may be seen by reference to the literature on the toxic effects of oxygen (p.163), divers breathing oxygen under conditions of raised atmospheric pressure may also suffer from acute psychological and emotional aberrations.

Caisson and tunnel workers are subject to the anxiety associated with any hazardous occupation. Although the incidence of caisson disease has been greatly reduced by protective measures, the "sandhog" realizes that he may suddenly lose consciousness even hours after leaving the caisson. These considerations have doubtless tended to deter anxious individuals from seeking employment in caisson and tunnel operations. As a class, caisson and tunnel workers are generally emotionally stable. As may be seen by consulting the section on the clinical picture of caisson disease (p. 115), mental symptoms may occur as a feature of decompression sickness but they are comparatively rare.

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1962. Will, O. A., Jr. Certain psychiatric reactions in operators of antisubmarine sound gear. *Nav. med. Bull., Wash.*, 1945, *44:* 746–748. [Ch]

Selection, Assessment of Efficiency, and Training of Submarine Personnel, Divers, and Compressed Air Workers

Most of the work on selection and training of submarine and diving personnel is to be found in unpublished reports, and these should be consulted by readers having access to the classified literature. The references cited below will serve to indicate certain aspects of the field of selection and training in general.

The importance of psychiatric factors in selection of submarine crews has been recognized for some time. At the U.S. Submarine Base, New London, Conn., psychological tests have been in use since 1941. Much of the work in this field during World War II has revolved about the application and evaluation of many already existing as well as new psychological aptitude tests. A significant feature of this work has been the utilization of self-administering group testing methods designed to screen out candidates lacking emotional stability and having psychopathic tendencies making them unfit for submarine duty. In addition to paper-and-pencil group tests, further screening has been possible through interviews with the personnel officer and, where necessary, by consultation with the psychiatrist.

The escape training tank has played an integral role in screening and selecting officers and men for submarine duty. Unusual emotional responses of candidates while taking the escape training or while under pressure serve as an aid in screening doubtful cases.

A most vital phase of selection is the need to fit the candidate to the wartime duty. Early in World War II, the lack of standardized tests to accomplish this was acutely felt. At present, active research is underway to fill this need.

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1970. Jones, R. F. Selection of personnel for submarines. *Nav. med. Bull., Wash.*, 1926, *24:* 461–476. [R]

1971. Lebensohn, Z. M. Psychoses in naval officers: a plea for psychiatric selection. *Amer. J. Psychiat.*, 1945 *101:* 511–516.

1972. Master, A. M. and E. T. Oppenheimer. A simple exercise tolerance test for circulatory efficiency with standard tables for normal individuals. *Amer. J. med. Sci.*, 1929, *177:* 223–243.

1973. Olivi, G. Idoneità fisica degli equipaggi dei sommergibili. *Ann. Med. nav. colon.*, 1913, *2:* 470–482.

1974. Regnault, J. Aptitude physique pour le service à bord des sous-marins. *Arch. Méd. Pharm. nav.*, 1905, *84:* 161–167. [P, R]

1975. Richter, A. B. Some practical considerations of cardiovascular examinations in youth. *J. Indiana med. Ass.*, 1945, *38:* 91–93.

1976*. Rozanov, L. S. [Selection of 18-19 year old workers for caisson work in subway construction.] *Klin. Med., Mosk.*, 1943, *21*(10): 74.

1977. Rutherford, E. D. Examination of candidates for submarine detector rating. *J. R. nav. med. Serv.*, 1921, *7:* 163–168.

1978. Shilling, C. W. Vital capacity and its relation to chest expansion. *Nav. med. Bull., Wash.*, 1933, *31:* 7–18.

1979. Shilling, C. W. and J. A. Hawkins. The hazard of caisson disease in individual submarine escape. *Nav. med. Bull., Wash.*, 1936, *34:* 47–52. [R]

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1980. Thwaytes, W. G. The influence of arterial hypertonus on the clinical estimation of blood-pressure, with some observations on the arteries of submarine ratings. *J. R. nav. med. Serv.*, 1919, *5:* 249–260. [P]

1980a. Anon. Submarine medical research. *Hosp. Cps. Quart.*, 1945, *18*(10): 19–24. [R]

Protection of Personnel

I. GENERAL STUDIES

Protection of personnel exposed to conditions prevailing in submarines, caissons, and underwater tunnels involves constant and close liaison between engineers and designers on the one hand and physiologists and medical officers, on the other, who are concerned with human factors as they affect and are affected by engineering design. In the sections which follow, a number of the protective devices and techniques for maintaining and restoring the health of personnel in submarines, caissons, and subaqueous tunnels will be discussed under specific headings. The present section is devoted to a few reports of general interest which will be referred to briefly. The first of these is a paper by Brodier (*1982*) published in 1919 on the hygiene of submarines. The paper is concerned with ventilation problems, specifically liberation of hydrogen sulfide and hydrogen from the batteries and the dangers associated with these gases. Absorption of carbon dioxide and the problem of cooking odors were also considered. Sanitary provisions, including toilet facilities, were discussed and the question of microorganisms in the air was raised.

Brown's report (*1983*) on the medical and hygienic aspects of the submarine service, published in 1920, may be consulted for a general survey of problems facing the biologist, medical officer, and engineer in dealing with the human factors in submarines. Brown discussed air-conditioning problems and referred also to the necessity of protecting the eyes of personnel doing electric welding.

Behnke's article (*1918*), published in 1941, on the medical aspects of submarine rescue and salvage efforts may be consulted for contributions to protection of personnel. The escape "lung" and training in its use were considered, as well as the dangers of rupture of the lungs in escape accidents. Oxygen therapy, particularly in nitrogen narcosis was discussed. Recompression procedures and the use of helium were also considered. In an article on health and habitability aboard submarines, published in 1944, Francis (*1985*) discussed air conditioning, preparation and serving of food, maintenance of morale, and the problem of leisure time.

In regard to the medical problems of divers, French (*1987*) 1915 discussed diving apparatus and the physics and physiology of diving. Carbon dioxide absorbents as well as accident prevention were also considered. A report of some interest in relation to the protection of divers is that of Coureaud (*1984*) 1923. This paper reviews a French regulation of September 16, 1922, according to which naval divers were to be subjected to medical examinations every 3 months. The maximum age for service was fixed at 45 years and medical examination was always to be carried out whenever divers contemplated a descent to depths greater than 35 m. In such cases, a medical officer was to be present. A special training was prescribed for divers. A diver was to be in good health and free of respiratory or cardiac affections and the nose and middle ear free of abnormality. He should not be suffering from any active constitutional disease and there should not be obesity. On ascent, the rate should not be so rapid as to incur danger of the "bends." An ascent rate of 4 to 5 m. per second from dives of less than 20 m. depth was suggested and the maximum time per day at the bottom was given as 7 hours. At 20 to 25 m., the total time of submergence in any 1 day should not exceed 6 hours, according to the author. For depths between 25 and 30 m., divers were not to

remain submerged for longer than a total of 4 hours a day and at depths of 35 to 40 m., the maximum time of daily submergence was set at 3 hours.

The author quoted decompression tables given in a regulation issued on July 27, 1912. In this regulation, it was stated that no serious accidents were likely to occur on ascent from depths of less than 20 m. It was recommended that decompression times be longer during longer stays at the bottom. Divers were advised to exercise on reaching the surface to facilitate disengagement of nitrogen bubbles. This suggestion has repeatedly been made in the literature but the practice is no longer recommended in deep diving. According to the French regulations of 1912 (see *1985*), if divers have been at depths of 20 to 30 m. for not longer than 5 minutes, the decompression time should be 1 m. per minute. For ascent from depths of more than 30 m., and if the stay on the bottom is more than 10 minutes, the time for ascent should be doubled. The total duration of decompression should always be proportional to the time spent on the bottom. The regulations recommended that no descents be made to depths greater than 45 m. unless absolutely necessary. It was recommended that at least a 1½-hour interval be allowed between ascent from one dive and a second descent. An automatic self-contained diving dress was discussed. In this dress, the diver was not dependent upon an air supply from the surface but carried an oxygen tank. Carbon dioxide was absorbed by potash solution. It was claimed that the suit would function for 4 hours.

A history of modern diving dress and a description of diving apparatus was given by Fraser (*1986*) 1939–40. Fraser also discussed the prevention of decompression sickness by inhalation of oxygen during decompression. Decompression tables were also given as well as a description of the submersible decompression chamber and oxygen breathing apparatus.

1981. Behnke, A. R. Medical aspects of submarine rescue and salvage efforts. *War Med., Chicago*, 1941, *1:* 168–179. [P, R]

1982. Brodier, L. Hygiène des sous-marins. *Paris méd.*, 1919, *34:* 298–303. [R]

1983. Brown, E. W. Medical and hygienic aspects of the submarine service. *Nav. med. Bull., Wash.*, 1920, *14:* 8–17. [P, R]

1984. Coureaud, H.-H.-L. L'hygiène des scaphandriers. *Arch. Med. Pharm. nav.*, 1923, *113:* 479–492. [R]

1985. Francis, W. S. Health and habitability aboard submarines. *Hosp. Cps. Quart.*, 1944, *17*(5): 52–56. [R]

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1987. French, G. R. W. Observations on deep diving. *Nav. med. Bull., Wash.*, 1915, *9:* 227–253. [R]

1988. Lockhart, J. C. *La viciación del aire en los submarinos.* Buenos Aires, 1935, 110 pp.

II. RADIUM, X-RAY, AND DENTAL THERAPY FOR OTITIS MEDIA

The problem of aerotitis media is one of particular concern not only in aviation personnel but also in divers. Susceptibility to the traumatic effects of pressure changes is increased by conditions which obstruct the Eustachian tube and prevent equalization of pressure within the middle ear. Lymphatic hyperplasia within the nasopharynx, coincidental with hyperplasia within the Eustachian tube, has been found to be a potent cause of Eustachian tube obstruction, and aviation personnel subjected to the cold, damp English climate have been victims of acute otitis media from this cause. Crowe and his associates, for a number of years, have been developing a technique for treating lymphatic hyperplasia in the nasopharynx by radium and radon irradiation. This technique has been applied to aviation personnel suffering from acute otic barotrauma with promising results.

A research program has for some time been underway at the U. S. Submarine Base in New London, Conn. to investigate the value of local radium therapy in the treatment and prevention of acute aerotitis media in personnel subjected to high pressures in the compression chambers in connection with submarine escape training. These studies are reported by Haines (*Ann. Otol., etc., St Louis*, in press). A total of 1,659 men contracted more or less severe aerotitis media when subjected to a

50-lb. pressure test. A total of 732 of these cases of aerotitis media were treated with radium. An attempt was made to administer radium at least 4 times in each case; in some cases as many as 8 treatments were needed. It was sometimes impossible to complete a series of 4 treatments when, for example, a man was unexpectedly transferred. But for the most part, therapy was completed and the man again admitted to the pressure chamber. Of these treated men, less than 10 percent exhibited aerotitis media when again subjected to the pressure test. A control group of 264 men who developed aerotitis media were given only symptomatic treatment. Over 90 percent of these men exhibited aerotitis media when again subjected to pressure.

For many years, X-rays have been used in the treatment of acute, subacute, and chronic otitis media and papers on this subject by Dionisio (*1992*) 1906, Beattie (*1989*) 1921, Raynal (*1998*) 1923, Grande (*1995*) 1925, Yocom (*2003*) 1925, Goldmann (*1994*) 1929, and Lucinian (*1996*) 1936 should be consulted. Murphy, Witherbee, Craig, Hussey, and Sturm (*1997*) 1921 reported treatment of hypertrophied tonsils by means of X-rays. It appears, however, that the use of X-rays for reducing lymphatic hyperplasia is not as effective in the prevention or treatment of otitis media as the use of radium. X-ray therapy has also been applied in the relief of acute mastoiditis and the reader will find reference to this treatment in reports by the following authors: Swanson (*2002*) 1939, Schillinger (*2001*) 1932, Ross (*2000*) 1932, Cherniak and Gorodetzky (*1990*) 1934.

A wholly different therapeutic attack on the problem of aerotitis media has been made by Kelly at the U. S. Submarine Base, New London, Conn. (*Ann. Otol., etc., St Louis*, in press). Success was reported by other workers in relieving ear symptoms in some aviators with overclosure of the mandible by inserting a splint between the back teeth to open the bite. This suggested to Kelly that the muscles concerned with jaw movement were also involved in some way with functions of the Eustachian tube. It was reasoned that any abnormally strained muscular activity during jaw movement might have a deleterious effect on tubal function. Accordingly, efforts were made to provide normal, unstrained muscle action during all jaw movements. Jaw movements of patients were studied from X-rays and casts of the jaws and the points on teeth which hampered excursions were corrected.

Fifty patients with severe aerotitis media and with interference of mandibular function were taken for dental treatment. Following treatment, the men were given a second pressure test. Forty-six patients came through the pressure chamber with normal, or grade O ears. This finding was based upon an examination of each ear with the otoscope in the hands of an experienced otologist. Three of the four unsuccessful cases yielded to radium therapy. One case resisted all efforts.

The results of 3 independent control groups confirmed the author's opinion that the success with these 46 patients might be directly referred to the dental treatment described. In explanation of the success of dental therapy in aerotitis media, it has been suggested that normally the action of the superior pharyngeal constrictor muscles stimulates the lymph vessels draining the Eustachian tube, and that dysfunction of that muscle may lead to stasis in the tube. The action of the buccinator muscle is intimately connected with the action of the superior pharyngeal constrictor muscle by way of the pterygomandibular raphe, and it was reasoned that the rationale of dental therapy lay in restoring normal unstrained functioning to the buccinator and hence to the superior pharyngeal constrictor. This was believed to reduce the abnormal tourniquet effect of the latter on the lymphatics and so restore the normal massaging effect, thereby stimulating lymphatic drainage and thus reducing congestion of the Eustachian tube.

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1994. Goldmann, R. Zur Röntgenbehandlung der akuten Entzündung der Mittelohrräume. *Strahlentherapie*, 1929, *33:* 152–155. [P]

1995. Grande, C. La cura delle otiti medie catarrali coi raggi Roentgen. *Arch. ital. Otol.*, 1925, *36:* 197–205. [P]

1996. Lucinian, J. H. Treatment of otitis media and mastoiditis by the Roentgen ray. Analysis of fifty consecutive cases. *Amer. J. Roentgenol.*, 1936, *36:* 946–953. [P, Ch]

1997. Murphy, J. B., W. D. Witherbee, S. L. Craig, R. G. Hussey, and E. Sturm. Induced atrophy of hypertrophied tonsils by Roentgen ray. *J. Amer. med. Ass.*, 1921, *76:* 228. [P]

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1999. Rentschler, H. D. and J. W. Settle. Treatment of impaired hearing by radiation of excessive lymphoid tissue in the nasopharynx. *Penn. med. J.*, 1944, *47:* 985–988.

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2001. Schillinger, R. The apparent therapeutic effect of the Roentgen ray upon the clinical course of acute mastoiditis. (Preliminary report.) *Radiology*, 1932, *18:* 763–776. [P]

2002. Swanson, C. A. Roentgen ray therapy of acute mastoiditis and acute otitis media. *Nav. med. Bull., Wash.*, 1939, *37:* 610–617. [P]

2003. Yocom, A. L. X-ray treatment of chronic otitis media. *Med. Her.*, 1925, *44:* 268–269. [P]

III. USE OF ULTRAVIOLET LIGHT FOR SUBMARINE CREWS

Much evidence has been collected on the action of ultraviolet light in destroying bacteria in air and water and in reducing the incidence of various airborne infections in human subjects. While it is true that artificial irradiation with ultraviolet light does have a sterilizing action on air and water, nevertheless, it is not yet possible to say that ultraviolet treatment of air in enclosed spaces will significantly reduce the incidence of infections, and as far as the value of ultraviolet irradiation in improving general health is concerned, it must be admitted that the evidence is not clear-cut.

Ultraviolet lamps have been installed experimentally in submarines but there are not yet enough data to make any statement for or against their efficacy.

Dalgleish (*2004*) 1940 reported experiments in which submarine crews were provided with ultraviolet lamps for 4 months. Crew members were permitted to expose themselves on alternate days to ultraviolet light. Fourteen men at a time took the treatment, exposing the back for 4 minutes and the front for 4 minutes. The data are admittedly incomplete but the author believed that efficiency was somewhat improved (particularly toward the end of a patrol), that there was less illness, and that morale was higher.

2004. Dalgleish, P. H. The use of artificial sunlight for submarine crews. *J. R. nav. med. Serv.*, 1940, *26:* 405–406. [P, R]

IV. VENTILATION; AIR CONDITIONING

A. GENERAL STUDIES

A number of early studies by Belli and his colleagues on air conditioning within submarines are worth consulting from a developmental and historical point of view. In 1907, Belli (*2005*) published a short note on alterations of the air in submarines on submergence. He reported that after 2 hours of submergence, the temperature rose 2° to 3° C., the humidity rose to about 85 percent, and the oxygen concentration dropped to 19 percent. There was a rise in the concentration of carbon dioxide in the air as well as an increase in the concentration of hydrogen sulfide and various volatile hydrocarbons. Belli and Trocello (*2009*) 1908 reported on the conditioning of the air in submarines. Figures were given of concentrations of oxygen, carbon dioxide, sulphuric anhydride, hydrogen sulphide, volatile hydrocarbons, carbon monoxide, ammonia, nitric acid, and chlorine. Similar studies were reported in 1912 by Belli and Olivi (*2008*). Marantonio (*2024*) 1917 discussed mechanical devices for ventilation and air renewal on the submarine *Ballila*. Ventilation of the storage batteries and electrical motors was considered

and also carbon dioxide absorption, supplementary oxygen supply, and addition of air for rescue purposes from the outside.

The reader is referred to a further article on submarine ventilation published in 1920 by Marantonio (*2025*). Two papers by Belli (*2006, 2007*) were published in English in 1922 and these may be consulted for details of construction of submarines from the point of view of habitability.

Jones and Mankin (*2019*) 1924 discussed submarine ventilation in tropical waters. They called attention to earlier work suggesting that the oxygen and carbon dioxide content of submarine air do not usually pass acceptable limits until after 17 hours of submergence. They stated that heat tends to be dissipated through the hull into the water and through ventilating lines in the superstructure. The temperature of the water was, therefore, recognized as an important factor in heat elimination. It was stated that the ship was always hotter during the day when surfaced because of the effect of the sun beating on the hull. Three experimental runs were made under various conditions to determine the habitability of the submarine. It was concluded that bad odor in the submarine lowered morale. The submarine odor was a composite smell made up of smells from the galley, oil smells, products of partial fuel combustion, and body odors. Inadequate toilet facilities were recognized as causing chronic constipation; bunking arrangements were considered insufficient. Arrangements for food storage were poor and ventilation was uncertain. Air conditioning in the torpedo compartments were found to be the worst. It was recommended that judicious placing of overhead fans throughout the submarine would facilitate the circulation of air and contribute to comfort. The authors suggested installation in submarines of air-conditioning systems. They stated that the conditions in the engine compartments were not as bad as they had expected them to be and that they were superior to conditions in some surface vessels. It was concluded that R-boats should be able to carry out regular 2-week patrols in tropical waters. In general, it was concluded that the circulation of air within the submarine should be increased, blowers should have an increased capacity, and more fans should be provided. Improved toilet facilities were considered highly essential. The authors believed that the ventilating systems for the living compartments should be separate from those for the engine and motor compartments.

For a detailed report of air conditions within submarines with particular reference to ventilation, the reader should consult part III of DuBois' long article (*2012*) published in 1928. With adequate ventilation, DuBois believed that submarines might remain submerged for periods of 96 hours or more without discomfort. The problem of carbon dioxide concentration in submarine air was discussed. The upper limit of carbon dioxide concentration for survival of human beings was given as about 8 percent. There is, however, marked distress if the concentration rises above 5 percent. A decrease of the oxygen concentration to as low as 6 to 7 percent causes immediate collapse. A gradual decrease in oxygen concentration can be withstood better than a sudden fall. The capacity for work performance and mental acuity both show a decrease with a fall in oxygen concentration and it was recommended that the oxygen concentration in submarine air ought not to fall below 17 percent. Hydrogen, though nontoxic, may form explosive mixtures with air unless the concentration of hydrogen is kept below 2 percent. DuBois stated that chlorine, which may reach the submarine air if sea water gets into the batteries, is annoying to personnel in concentrations of 1 part per million and dangerous in concentrations of 10 parts per million. Sulphuric acid fumes, although annoying, were not considered dangerous. Arsene, stibine, carbon monoxide, and gasoline fumes were discussed. DuBois reviewed various procedures for testing the concentrations of these substances in air. He also discussed the removal of carbon dioxide with caustic soda, caustic potash, and soda lime. Of these three carbon dioxide absorbents, soda lime was considered the most efficient. The supply of oxygen to submarines by means of cylinders and the possibility of using liquid

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oxygen were mentioned. Reduction of humidity, neutralization of chlorine, oxidation of arsene, and absorption of carbon monoxide were all discussed.

In a paper published in 1928 on submarine habitability, Carpenter (*2010*) stated that ventilation and air purification are important in submarines not only from a strictly medical point of view but also from the standpoint of efficiency of performance. On S-boats and some R-boats, ventilation was maintained by passing air in a trunk line beneath the deck and over the hull so that it was cooled by the sea water. Two blowers acted as supply or exhaust, circulating air at a rate sufficient to effect a complete change of air every 20 minutes. In German submarines at the time of Carpenter's report, it was stated that there were two main air trunks; the gallies had air supply and exhaust; the heads were provided with exhaust; and the store rooms had either exhaust or air supply. In the German submarines, the officers' quarters had an air supply and the crew quarters and battery compartments had both supply and exhaust. Theoretically, according to Carpenter, air ducts should be placed to give most space in living quarters and there should be drains to conduct water of condensation from ventilating trunks into the bilge. Two lines were considered costly in space and weight but gave much better ventilation. It was recommended that battery rooms have separate ventilation. Regarding human tolerance to high carbon dioxide concentrations in submarines, Carpenter stated that while carbon dioxide concentrations as high as 3 percent did not cause acute effects, continued exposure to concentrations lower than this might result in listlessness and "dopiness" amongst the crew. Occasional addition of oxygen to the submarine air tended to improve the condition of the men. It was stated that personnel could ***survive*** in oxygen concentrations as low as 7 percent. In German submarines, it was reported that oxygen was supplied to the air after 10 hours of submergence and that submarines carried devices for carbon dioxide estimation. Carbon dioxide absorbent requirements were discussed. One kilogram of soda lime is capable of absorbing 400 grams of carbon dioxide in 24 hours from an atmosphere containing 2 to 8 percent carbon dioxide. Recommendations concerning illumination, toilet facilities, and cooking arrangements were made. It was advised that mechanical refrigerators be made available for food and drinking water. Drinking fountain outlets were recommended for every compartment and it was advised that each member of the crew be provided with a gas mask to reduce the danger of chlorine in case of an accident to the battery compartment. Special diseases encountered in submarine personnel were discussed.

A number of reports dealing with general problems of ventilation have been selected from the large literature on air conditioning as being of possible application to the problems as encountered in the submarine service. According to Flügge (*2014*) 1905, the ill effects of confined spaces are not due to the exhalations of the occupants but are to be attributed to other causes, notably the heat evolved. Conversely, the healthful effect of fresh air lies more in its cooling power than in its chemical purity. These observations appear to be valid in crowded rooms in which there is little actual change in the oxygen and carbon dioxide concentrations. However, in submarines, the composition of the air may be so altered as to be irrespirable. According to Paul (*2028*) 1905, human subjects breathing air in a confined space suffered no ill effects even when the carbon dioxide concentration reached 16 parts per thousand, until the temperature rose above 25°C. and the humidity exceeded 50 percent. There was then headache, confusion, oppression, and dizziness.

According to Henderson (*2016*) 1912–13, temperature and moisture of the air are controlling factors in the effects of air on bodily comfort.

For a review of physiological effects of atmospheric conditions from the point of view of ventilation problems, the reader should consult reports by Miller (*2026*) 1917, and MacLeod (*2022*) 1920. In 1922-23, Hill (*2017*) published a plea for clean air in ships, factories, mines, and submarines. It was reported that

in submarines, confined air can be endured until the concentration of carbon dioxide reaches 3 percent, the oxygen concentration being correspondingly diminished. Hill made the statement that close, vitiated air favored the spread of airborne infection.

In 1929, Mañosa (*2023*) discussed the problem of ventilation in the tropics with special reference to climatic conditions prevailing in Manila. This paper may be consulted for a brief historical description of the theories proposed to explain the ill effects of bad ventilation. As Mañosa stated, Lavoisier in 1877 attributed the symptoms arising from exposure to close spaces to lack of oxygen. Pettenkofer in 1863 believed that carbon dioxide was not the cause of ill effects in badly ventilated rooms since the concentration of this gas never rose high enough to cause damage. The toxic action of vitiated air was said to be due to the presence of organic substances excreted by the body. Manosa concluded his report by a description of the bodily changes which take place in subjects exposed to heat and humidity and made sugestions for ventilation procedures.

For other general reports on air conditioning, the reader may consult articles by Govan (*2015*) 1931; Nakamoto, Fujino and Takahashi (*2027*) 1931; Loriga (*2021*) 1933; Sugioka (*2031*) 1936; Kossak (*2020*) 1937; Chapple (*2011*) 1938; and Stiening (*2030*) 1944.

2005. Belli, C. M. Les altérations de l'air dans les sousmarins. Note préliminaire. *Int. Congr. Hyg.* (*Demogr.*), 1907, *14*(4): 718–719. [P]

2006. Belli, C. M. Hygiene of submersibles. Part I. *Nav. med. Bull., Wash.*, 1922, *17:* 589–611. [P, R]

2007. Belli, C. M. Hygiene of submersibles. Part II. *Nav. med. Bull., Wash.*, 1922, *17:* 785–802. [P, R]

2008. Belli, C. M. and G. Olivi. L'aria nei sommergibili immersi. *Ann. Med. nav. colon.*, 1912, *2:* 489–531. [P]

2009. Belli, C. M. and E. Trocello. Viziamento e rinnovamento dell'aria nei sottomarini. *Ann. Med. nav. colon.*, 1908, *14*(1): 1–26. [P]

2010. Carpenter, D. N. Habitability of submarines. *Nav. med. Bull., Wash.*, 1928, *26:* 31–40. [R]

2011. Chapple, C. C. An incubator for infants. *Amer. J. Obstet. Gynec.*, 1938, *35:* 1062–1065.

2012. DuBois, E. F. Physiology of respiration in relationship to the problems of naval medicine. Part III. Submarine ventilation. *Nav. med. Bull., Wash.*, 1928, *26:* 515–552. [R]

2013. Fernández-Cuesta y Porta, N. Desinfeccion de buques sumergibles. *Atti Congr. int. Med. Farm. milit.*, 1923, *2:* 478–480. [P, R]

2014. Flügge, C. Ueber Luftverunreinigung, Wärmestauung und Lüftung in geschlossenen Räumen. *Z. Hyg. InfektKr.*, 1905, *49:* 363–387. [P]

2015. Govan, J. Extent of air conditioning requirement from the standpoint of hospital administration. *Bull. Amer. Hosp. Ass.*, 1931, *5*(10): 122–130.

2016. Henderson, Y. A consideration of the unknown factors in the ill-effects of bad ventilation. *Biochem. Bull.*, 1912–13, *2:* 146–147. [P, R]

2017. Hill, L. Clean air. *J. R. sanit. Inst.*, 1922-23, *43:* 67–81. [R]

2018. Hirsch, M. Wie lassen sich bei der Belüftung von Fabrikationsräumen Ware und Arbeiter unterschiedlich berücksichtigen *Zbl. GewHyg.*, 1927, N. Folge, *4:* 69–70. [R]

2019. Jones, R. F. and G. H. Mankin. Studies of submarine ventilation in tropical waters. *Nav. med. Bull., Wash.*, 1924, *20:* 759–795. [P, R]

2020. Kossak, W. Klimaanlagen, Konstruktions- und Betriebsfragen. *Z. GewHyg.*, 1937, *44:* 143–155; 166–171.

2021. Loriga, G. Il lavoro in atmosfera chiusa e condizionata. *Rass. Med. Lav. industr.*, 1933, *4:* 1–11.

2022. MacLeod, J. J. R. On ventilation. *Publ. Hlth J., Toronto*, 1920, *11:* 101–118. [R]

2023. Mañosa, M. The problem of ventilation in the tropics with particular reference to the climatic conditions of Manila, *Rev. filipina Med.*, 1929, *20:* 90–101. [R]

2024. Marantonio, R. Mechanical devices for ventilation and air renewal on the submarine "Ballila." *Nav. med. Bull., Wash.*, 1917, *11:* 156–175. [P]

2025. Marantonio, R. Sulla ventilazione delle navi sommergibili. *Ann. Med. nav. colon.*, 1920, *2:* 467–486. [P]

2026. Miller, J. A. Some physiological effects of various atmospheric conditions. *Amer. J. med. Sci.*, 1917, *153:* 412–420. [P, R]

2027. Nakamoto, T., S. Fujino, and H. Takahashi. Air condition on board the battle-ship "Fuso" in summer. *Bull. nav. med. Ass. Japan*, 1931, *20*(6): (English text pagination), 1–2. (In Japanese with English summary.)

2028. Paul, L. Die Wirkungen der Luft bewohnter Räume. *Z. Hyg. InfektKr.*, 1905, *49:* 405–432.

2029. Schmitz, N. A. [Caisson air from the hygienic stand-point.] *Vrach, Spb.*, 1887, *8:* 847–849; 870–871.

2030. Stiening, F. H. Air conditioning. Factors affecting human comfort: fundamental requirements of an air conditioning system. Pp. 148–155 in: *Introduction to Industrial Medicine*. Edited by T. Lyle Hazlett. Pittsburgh, University of Pittsburgh, 1944, 216 pp. [R]

2031. Sugioka, N. On the estimation of air ion in the war ships and the influence of anion on the fatigue of the crew. *Bull. nav. med. Ass. Japan*, 1936, *25*(5): (English text pagination), 25. (In Japanese with English summary.)

B. TOXIC NATURE OF EXHALATIONS FROM THE LUNGS

In 1883, Hermans (*2036*) discussed the cause of discomfort and illness in closed rooms. Questioning the theory of oxygen lack as a factor, Hermans referred to previous investigations of the physiological and pathological effects of low oxygen concentration but concluded that in crowded rooms, the oxygen concentration seldom falls below 20 percent. He stated also that in closed rooms in ordinary living quarters, the carbon dioxide concentration rarely exceeds 1 percent. Experiments on animals and human subjects were quoted indicating tolerances of carbon dioxide in concentrations much higher than 1 percent. Concerning the danger of toxic organic substances exhaled by the occupants of a confined space, the author carried out experiments which indicated that no such substances were given off by human subjects in confined chambers. In one experiment, a man was placed in a small chamber for 24 hours with no apparent ill effects. In a second chamber (1.8 by 0.75 by 1.2 m.) one or two persons were confined for 8 hours. If excess carbon dioxide was not removed, there was an increase in respiratory rate but no organic substances were produced. Hermans concluded that it was the rise in temperature of the room or increase in humidity which caused discomfort and that the only possible exhalation of vapors or odors would be those coming from unclean bodies, clothing, or from skin wounds.

For many years, it was believed that expired air contained some volatile toxic substance or substances and that it was the liberation of these products into the air that rendered air in unventilated spaces unhealthful. This view rested largely upon experiments of Brown-Séquard and d'Arsonval (*2032*, *2033*, *2034*) 1887 and 1888. These investigators reported that condensation fluid from human pulmonary exhalations could kill pigeons, guinea pigs, or rabbits when injected rectally, subcutaneously, or intravenously, or when taken orally. A guinea pig died in less than 11 hours after injection of 3 cc. of such liquid into the peritoneal cavity. When injected into the lungs, the fluid caused marked congestion followed by a true inflammatory reaction. Brown-Séquard and d'Arsonval did not believe that it was the water itself that caused death when injected intravenously and they called attention to the fact that Claude Bernard and Paul Bert had injected water into the respiratory tract without harm and that Magendie and Bouchard had injected water intravenously with no harmful effects. Moreover, subcutaneous injection of the pulmonary condensate was apparently lethal. The authors raised the question of whether the condensate derived its lethal properties from contamination by laboratory air or whether the poisonous factor came from putrifying material between the teeth or in the buccal cavity. They believed that this was not the case since the condensate was collected by means of a tracheal cannula.

Contradictory results were reported in 1888 by Dastre and Loye (*2035*). Dogs breathed air from a closed chamber vitiated by another animal. Also, condensation products of respiration from one animal were introduced into the blood stream of another animal. In the first type of experiment, air from one dog was breathed by another for 6½ hours with no harmful effects, immediate or delayed. In the second type of experiment, condensation products from the lungs of one dog were injected intravenously into another dog. A similar experiment was carried out in rabbits. In most cases, there was no harmful effect. Dastre and Loye concluded that the respiratory surfaces probably did not liberate a toxic substance into the expired air.

As late as 1912, claims were made for a toxic organic substance in exhaled air. Rosenau and Amoss (*2037*) 1911–12 took the condensed moisture from human expired air and injected this liquid into guinea pigs. After a suitable interval, the guinea pigs were injected with normal human serum. Twenty-six out of twenty-nine animals showed definite symptoms of anaphylaxis. Four of

these died in anaphylactic shock and it was concluded that an organic protein-like substance is excreted in the breath.

The fact that submarine personnel can survive and remain healthy for long periods of time while submerged, providing that conditions of temperature, humidity, oxygen supply, and carbon dioxide content of the air are maintained within reasonable limits, furnishes very satisfactory proof that for practical purposes, the exhalation of such toxic or organic substances via the lungs need not be considered a hazard.

2032. Brown-Séquard, [ ] and [ ] d'Arsonval. Démonstration de la puissance toxique des exhalaisons pulmomaires provenant de l'homme et du chien. *C. R. Soc. Biol. Paris*, 1887, Sér. 8, *4:* 814–818. [C, P]

2033. Brown-Séquard, [ ] and [ ] d'Arsonval. Toxicité de l'air expiré; nouvelles recherches. *C. R. Soc. Biol. Paris*, 1888, Sér. 8, *5:* 90–91. [C, P]

2034. Brown-Séquard, [ ] and [ ] d'Arsonval. Remarques sur la valeur des faits qui nous ont servi a démontrer la toxicité de l'air expiré. *C. R. Soc. Biol. Paris*, 1888, Sér. 8, *5:* 99–104. [C, P]

2035. Dastre, A and P. Loye. Recherches sur la toxicité de l'air expiré. *C. R. Soc. Biol. Paris*, 1888, Sér. 8, *5:* 91–99. [C, P]

2036. Hermans, J. T. H. Ueber die vermeintliche Ausathmung organischer Substanzen durch den Menschen. Ein Beitrag zur Ventilationsfrage. *Arch. Hyg., Berl.*, 1883, *1:* 5–40. [P, R]

2037. Rosenau, M. J. and H. L. Amoss. Organic matter in the expired breath. *J. med. Res.*, 1911–12, N. Ser., *20:* 35–84. [P]

C. AIR FLOW AND VOLUME

The volume of air required within enclosed spaces for maintenance of health in personnel and the rate of circulation of the air are factors which are of importance in designing submarines and air-conditioning systems. These factors have been satisfactorily worked out for durations of patrol and times of submergence imposed by tactical needs as they existed in World War II. New developments in submarine design and technical devices for introducing air into submarines will permit far longer periods of submerged operation in the future. It will continue to be important, therefore, to give attention to the effects of raised carbon dioxide concentrations on submarine personnel under conditions of operation and it is seriously recommended that field as well as laboratory research on this subject be continued. The reader will find references to the existing literature under the section on physiological effects of low oxygen and high carbon dioxide concentration (p. 51). Reference may also be made to an early paper published in 1873 by de Ranse (*2040*) on the volume of air necessary for health.

de Pulligny (*2039*) 1908 reported that at depths up to 20 m., divers do well providing they received 50 to 100 liters of air per minute. At 40 to 45 m., diving operations with air were troublesome whatever volume of air is supplied. de Pulligny reviewed previous studies on air requirements for divers.

For charts showing effective temperature at different humidities with various air velocities, the reader should consult a study by Houghten and Yagloglou (*2038*) 1924 on the cooling effect on human beings produced by various air velocities.

2038. Houghten, F. C. and C. P. Yagloglou. Cooling effect on human beings produced by various air velocities. *Trans. Amer. Soc. Heat. Vent. Engrs.*, 1924, *30:* 193–212. [P]

2039. Pulligny, L. de. Les scaphandriers et la ventilation. *Ann. Hyg. publ., Paris*, 1908, Sér. 4, *10:* 143–146. [P, R]

2040. Ranse, F. de. Note sur l'espace cubique et sur le volume d'air nécessaires pour assurer la salubrité des lieux habités. *Gaz. méd. Paris*, 1873, Sér. 4, *28:* 445–446.

D. CARBON DIOXIDE ABSORPTION AND CARBON DIOXIDE ABSORBENTS; TOLERABLE CONCENTRATIONS OF CARBON DIOXIDE AND OXYGEN

Davy (*2048*) in 1818 published observations on the state of air in the fever hospitals of Cork, Ireland, at a time when they were crowded with patients suffering from infectious diseases. It was found that the vitiated air of such hospitals did not vary in concentration from the outside air. Reference may be also made to a study by Benedicenti (*2046*) 1900 on the concentration of oxygen, carbon dioxide, and other gases in railway tunnel air. Belli (*2045*) 1905, in a report on hygiene in submarines, referred to the use of sodium peroxide which both liberated

oxygen and absorbed carbon dioxide. According to this author, normal subjects consumed 25 liters of oxygen per hour and exhaled 23 liters of carbon dioxide in the same period of time. Additional oxygen might be supplied by the use either of compressed air or compressed oxygen.

Tanks of compressed oxygen add weight to the submarine and at present oxygen is mainly used for emergency purposes. It has been found that for periods of submergence necessitated by combat conditions encountered in World War II, the oxygen concentration did not fall to irrespirable levels. Similarly, carbon dioxide absorbents have not been used routinely. Although these absorbents may be introduced into the ventilation system, in most cases they are simply scattered in a thin layer in various parts of the submarine. In German submarines, large supplies of carbon dioxide absorbent were carried on board. This was necessitated by the prolonged periods during which these submarines were absent from their bases and the extended periods of submerged operation contemplated.

Many carbon dioxide absorbents have been tried and adopted. For many purposes, soda lime is satisfactory and has been used in various circumstances to absorb carbon dioxide in confined atmospheres. Laur (*2053*) 1917 reported that 5 kg. of soda lime spread over 1 sq. m. of surface is sufficient to absorb the carbon dioxide and water vapor from a room of 100 cu. m. Under the conditions of Laur's experiments, the soda lime retained its efficacy for 10 to 12 days.

For further reports on absorption of carbon dioxide, the reader may consult papers by Rideau (*2056*) 1919, Moteki (*2054*) 1926–27, Carstens-Johannsen (*2047*) 1927, Jardin (*2050*) 1938, Jean (*2051*) 1938, and Oudard (*2055*) 1939. In a small French submarine with a crew of 33, Oudard reported a concentration of 3 percent carbon dioxide at the end of 18 hours' submergence. The oxygen fell to a concentration of 18 percent. The carbon dioxide was absorbed by use of caustic soda and oxygen was added when the concentration of this gas fell below 17 percent.

According to Kilborn (*2052*) 1941, "Baralyme" has certain advantages over soda lime: It has a greater carbon dioxide absorbing power; it has a continuous action up until the period of exhaustion, requiring no "rest" periods; it is noncaustic; less heat is generated in the process; it has an average life which is 35 percent longer than soda lime per unit of volume; and no unpleasant odor is emitted during its use.

Batten and Adriani (*2044*) 1942 have reported clinical and experimental studies of the use of "Baralyme" for carbon dioxide absorption in anesthesia. This absorbent consists of one part of $Ba(OH)_2 \cdot 8H_2O$ plus 5 parts of $Ca(OH)_2$ made up in the form of pellets. Its advantages as an absorbent are also outlined by Batten and Adriani; however, these authors raised the question of the possible toxicity of the barium ion and believed that it may cause a rise of blood pressure and may of itself cause hyperpnea.

The reader will find a brief consideration of the history of carbon dioxide absorbing agents in a report by Batten (*2043*) published in 1943. The advantage of "Baralyme" are further discussed. Carbon dioxide absorption appliances are also described by Adriani and Byrd (*2042*) 1941 and Adriani and Batten (*2041*) 1942.

The carbon dioxide absorbent now in use in the submarines of the U. S. Navy is lithium hydroxide. This compound is highly caustic but it is efficient. As stated above, carbon dioxide absorbents are not used routinely in U. S. submarines but are carried for emergency purposes. The carbon dioxide concentration of the submarine air can be effectively reduced by spreading the absorbent thinly over tables and other flat surfaces.

2041. Adriani, J. and D. H. Batten. The efficiency of mixtures of barium and calcium hydroxides in the absorption of carbon dioxide in rebreathing appliances. *Anesthesiol.*, 1942, *3:* 1–10.

2042. Adriani, J. and M. L. Byrd. A study of carbon dioxide absorption appliances for anesthesia: the canister. *Anesthesiol.*, 1941, *2:* 450–455.

2043. Batten, D. H. The absorption of carbon dioxide from anesthesia apparatus. *N. Y. St. J. Med.*, 1943, *43:* 539–544. [M]

2044. Batten, D. H. and J. Adriani. Clinical and experimental studies of barium and calcium hydroxide mixtures (baralyme) for carbon dioxide absorption in anesthesia. *Curr. Res. Anesth.*, 1942, *21:* 151–158. [M]

2045. Belli, C. M. Hygienische Betrachtungen über unterseeische Schiffe. *Arch. Schiffs- u. Tropenhyg.*, 1905, *9:* 341–345. [P, R]

2046. Benedicenti, A. L'air dans le tunnel du chemin de fer de Ronco. *Arch. ital. Biol.*, 1900, *34:* 361–365.

2047. Carstens-Johannsen, E. Ventilation och luftrening å undervattensbåtar. *Tidskr. milit. Hälsov.*, 1927, *52:* 16–23.

2048. Davy, E. Experiments and observations upon the state of the air in the fever hospitals of Cork, at a time when they were crowded with patients, labouring under febrile contagion. *Lond. med. phys. J.*, 1818, *39:* 274–277.

2049. Glibert, [ ]. Le bilan pathologique du travail à domicile. *Bull. Ass. belge Méd. soc.*, 1913, *1:* 4–13.

2050. Jardin, Édouard. *Contribution à l'étude toxicologique de l'air.* Thèse (Méd.) Paris, Jouve & Cie, 1938, 88 pp. [M, B]

2051. Jean, M.-L. La régénération des atmosphères confinées, au moyen de la soude. *Arch. Méd. Pharm. nav.*, 1938, *128:* 84–128.

2052. Kilborn, M. G. Preliminary clinical report on a new carbon dioxide absorbent—baralyme. *Anesthesiol.*, 1941, *2:* 621–627. [M]

2053. Laur, F. Régénération des atmosphères confinées. Étude sur la chaux sodée et sa régénération. *Rev. Hyg. Police sanit.*, 1917, *39:* 421–430.

2054. Moteki, K. Experimental studies on the method of removal of moisture and carbon-dioxide in the air of room. *Bull. nav. med. Ass. Japan*, 1926–27, *15*(4): (English text pagination), 8. (In Japanese with English summary.)

2055. Oudard, [ ]. La vie à bord des sous-marins. *Bull. Acad. Méd. Paris*, 1939, *121:* 693–699. [R]

2056. Rideau, [ ]. Considérations hygiéniques sur l'escadrille des sous-marins de Bretagne. *Arch. Méd. Pharm. nav.*, 1919, *108:* 94–108.

2057. Zuntz, N. Ventilation in confined quarters. *Rep. Brit. Ass.*, 1911, pp. 543–544.

E. TEMPERATURE CONTROL

Various types of refrigeration equipment for use in air conditioning have been described by Nusbaum (*2063*) 1917. The reader may also consult a paper by Sproule (*2065*) 1933 on air-cooling systems. A detailed description of air-conditioning apparatus is, however, not appropriate here and the reader should refer to articles on this subject in engineering journals and works on ventilating engineering. The physiological requirements of temperature and humidity are, however, of importance and certain reports on this subject are included. Hill and Campbell (*2060*) published a paper in 1922–23 on the cooling power of the atmosphere and comfort during work. It was considered that the efficiency of the body is not improved by moving it from an environment with a katathermometer cooling power of 3.9 to one of 11.2 millicalories per cm. per sec. However, the pulse rate is much reduced and body comfort greatly increased by this change. Hill and Campbell believed that there was a less rapid onset of fatigue and less strain upon the heart. As Yagloglou (*2068*) 1924 has stated, the constancy of the body temperature is maintained at the expenditure of energy. Yagloglou gave tables of heat production and heat loss for men of various sizes and various occupations. These tables may be of use to those wishing to determine the requirements of air conditioning in submarines.

Information concerning maximum comfort in moving air may be obtained from a paper by Yagloglou and Miller (*2073*) 1924. The effect of clothing in relation to effective temperature was discussed by Yaglou and Miller (*2074*) 1925. The effective temperature index was discussed by Yaglou (*2069*) 1926. According to Yaglou (*2071*) 1927, the comfort zone for men stripped to the waist lies between 66° F. and 82° F. effective temperature, the optimum probably being about 72.5° F. Pulse rate, rectal temperature, skin temperature, and basal metabolism all rise when the effective temperature increases. Between 40° and 75° F. effective temperature, the capacity for work remains constant while from 75° to 80° F., there is a slow decrease in work capacity. At levels above 80° F. effective temperature, there is a rapid decrease in capacity for work. Air movement increases comfort up to 99° F. effective temperature. Above this, it adds to discomfort.

Vernon (*2067*) 1926 considered that methods of determining effective temperature disregard the factor of acclimatization. He believed that the sensation of comfort depends upon air velocity as well as temperature.

Cooling power of air was thought to be a better index of comfort than effective temperature, since this agrees more closely with subjective body sensations.

For a discussion of the value and defects of the katathermometer, the reader should consult a paper by McConnell and Yagloglou (*2062*) 1924. In 1926, Yaglou (*2070*) discussed effective temperature versus the katathermometer as an index of comfort. This article is a point by point reply to Vernon's paper (*2067*).

2058. Anderson, R. A. Notes on air conditioning in the tropics. *J. R. Army med. Cps.*, 1933, *61:* 242–249.

2059. Hill, L. Discussion on ventilation in confined quarters, especially in relation to ships. *Rep. Brit. Ass.*, 1911, pp. 541–543. [R]

2060. Hill, L. and J. A. Campbell. Cooling power of the atmosphere and comfort during work. *J. industr. Hyg.*, 1922–23, *4:* 246–252. [P, R]

2061. Kaczorowski, [ ] von. Nachtrag zu dem Artikel: Die kalte Luft als Antipyreticum und Antisepticum. *Dtsch. med. Wschr.*, 1879, *5:* 644–645.

2062. McConnell, W. J. and C. P. Yagloglou. The kata thermometer: its value and defects. *Publ. Hlth. Rep., Wash.*, 1924, *39:* 2293–2307. [P, R]

2063. Nusbaum, L. The use of refrigeration in air conditioning. *Trans. Amer. Soc. Heat. Vent. Engrs.*, 1917, *23:* 671–678. [R]

2064. Reichenbach, H. and B. Heymann. Untersuchungen über die Wirkungen klimatischer Faktoren auf den Menschen. I. Mitteilung: Beziehungen zwischen Haut- und Lufttemperatur. *Z. Hyg. InfektKr.*, 1907, *57:* 1–22.

2065. Sproule, J. C. Report on an air cooling plant installed in the Haffkine Institute, Parel, Bombay, and the carrier cooling plant installed in the New Council Hall, Bombay. *J. R. Army med. Cps.*, 1933, *61:* 249–256.

2066. Vernon, H. M. Is effective temperature or cooling power the better index of comfort? *J. industr. Hyg.*, 1926, *8:* 392–401. [R]

2067. Vernon, H. M. Methods of investigating ventilation. *J. State Med.*, 1926, *34:* 144–153. [R]

2068. Yagloglou, C. P. The heat given up by the human body and its effect on heating and ventilating problems. *Trans. Amer. Soc. Heat. Vent. Engrs.*, 1924, *30:* 365–376. [P, R]

2069. Yaglou, C. P. The thermal index of atmospheric conditions and its application to sedentary and to industrial life. *J. industr. Hyg.*, 1926, *8:* 5–19. [P, R]

2070. Yaglou, C. P. Effective temperature versus Kata-thermometer: a reply to H. M. Vernon. *J. industr. Hyg.*, 1926, *8:* 402–413. [P]

2071. Yaglou, C. P. Temperature, humidity, and air movement in industries: the effective temperature index. *J. industr. Hyg.*, 1927, *9:* 297–309. [P, R]

2072. Yaglou, C. P. and K. Dokoff. Calibration of the Kata-thermometer over a wide range of air conditions. *J. industr. Hyg.*, 1929, *11:* 278–291. [P]

2073. Yagloglou, C. P. and W. E. Miller. Effective temperature applied to industrial ventilation problems. *Trans. Amer. Soc. Heat. Vent. Engrs.*, 1924, *30:* 339–364. [P, R]

2074. Yaglou, C. P. and W. E. Miller. Effective temperature with clothing. *Trans. Amer. Soc. Heat. Vent. Engrs.*, 1925, *31:* 89–99. [P, R]

F. HUMIDITY CONTROL

It is not intended under this heading to include in its entirety the extensive literature on methods of regulating humidity. The reader should consult reports such as that by Baldwin (*2075*) 1922 for information on the processes for mechanically drying and cleaning air. Other references are included without comment.

2075. Baldwin, W. J. Improvements in the process for drying and cleaning air mechanically. *Trans. Amer. Soc. Heat. Vent. Engrs.*, 1922, *28:* 7–10.

2076. Buxton, P. A. Control of humidity of air currents. *Nature, Lond.*, 1931, *128:* 837.

2077. Drinker, P. and R. M. Thomson. Experiments in air conditioning. *J. industr. Hyg.*, 1922–23, *4:* 63–69. [P, R]

2078. Hausbrand, E. Das spezifische Gewicht der Dampfluftmischungen bei Lufttrocknungsanlagen. *Gesundheitsing.*, 1921, *44:* 107–110. [P, R]

2079. Muntner, S. Über Luftbefeuchtung. *Gesundheitsing.*, 1926, *49:* 194–195; 209–217.

2080. Nothwang, F. Luftdruckerniedrigung und Wasserdampfabgabe. *Arch. Hyg., Berl.*, 1892, *14:* 337–363.

2081. Rubner, M. and [ ] von Lewaschew. Ueber den Einfluss der Feuchtigkeitsschwankungen unbewegter Luft auf den Menschen während körperlicher Ruhe. *Arch. Hyg., Berl.*, 1897, *29:* 1–55. [R]

2082. Seth, J. B. A method of obtaining air currents of different humidities. *Nature, Lond.*, 1931, *128:* 638–639.

2083. Yaglou, C. P. Sanitary aspects of air conditioning. *Amer. J. publ. Hlth.*, 1938, *28:* 143–147. [R]

G. ELIMINATION OF DUST, GASES, SMOKE, AND FUMES FROM AIR

The ventilation problems in submarines and caissons include the question of removal of smoke, fumes, and other impurities. Such

impurities are required by the air-conditioning system and there does not appear to be any published comment upon the medical aspects of this particular subject in the literature dealing with submarines. For related articles, the reader may wish to consult reports by Ohmes (*2091*) 1916; Desgrez, Guillemard, and Savès (*2086*) 1920; Beth (*2085*) 1921; Hoyer (*2089*) 1922; Murphy (*2090*) 1927; Green (*2087*) 1931; Arnaoutow and Weller (*2084*) 1932; and Hayhurst (*2088*) 1933.

2084. Arnaoutow, G. D. and E. W. Weller. Procedure for establishing optimum air conditions for light and heavy work. *J. industr. Hyg.*, 1932, *14:* 117–131.

2085. Beth, W. Die Reinigung von Luft und anderen Gasen von mechanischen Beimengungen. *Gesundheitsing.*, 1921, *44:* 78.

2086. Desgrez, [ ], [ ] Guillemard, and [ ] Savès. Sur l'assainissement de l'air souillé par certains gaz toxigues. *C. R. Acad. Sci., Paris*, 1920, *171:* 1177–1179.

2087. Green, H. W. The amelioration of atmospheric pollution. *Amer. J. publ. Hlth.*, 1931, *21:* 237–241.

2088. Hayhurst, E. R. Air-conditioning with relation to comfort, health, and efficiency. *J. industr. Hyg.*, 1933, *15:* 98–115.

2089. Hoyer, F. Über Luftentstaubungsvorrichtungen. *Gesundheitsing.*, 1922, *45:* 398–401.

2090. Murphy, H. C. Design and application of oil coated air filters. *Trans. Amer. Soc. Heat. Vent. Engrs.*, 1927, *33:* 73–80.

2091. Ohmes, A. K. Clean, pure air for our cities. *Trans. Amer. Soc. Heat. Vent. Engrs.*, 1916, *22:* 471–477.

2092. Anon. Air impurities and ventilation in submarines. *Nav. med. Bull., Wash.*, 1922, *16:* 343–344. [R]

H. DISINFECTION OF THE AIR

Many procedures have been suggested for removing bacteria from air. For example, Trillat and Fouassier (*2107*) 1914, exposed room air to irradiation from a sample of pitchblende. The bacterial content was greatly reduced in certain tests but not all results were equally striking. d'Arsonval, Bordas, and Touplain (*2097*) 1920 reported that an electric spark had a sterilizing action on air. Cambier (*2096*) 1929 attempted to sterilize confined air with a quartz mercury vapor lamp. Ultraviolet light was reported by Wells (*2110*) 1935 to be effective in destroying colon bacilli introduced experimentally into an unconditioned air space. Wells and Fair (*2113*) 1935 discovered that irradiation of a room before spraying the bacteria into the air had no effect upon subsequent baterial count. According to Wells and Brown (*2112*) 1936, irradiation of the room with the quartz mercury vapor lamp after dissemination of influenza virus had a lethal effect on the organisms. Wells and Wells (*2114*) 1936 published a review of the subject of airborne infection which is of interest to those concerned with purification of submarine air. Methods of purification of room air were discussed in 1938 by Wells and Wells (*2115*).

The question of the use of aerosols for atmospheric and surface sterilization was discussed by Pulvertaft, Lemon, and Walker (*2103*) 1939. They pointed out that air purification by phenol sprays is ineffective and that ultraviolet light has a limited use. Many substances may be used as aerosols, some being more effective than others. Pulvertaft and Walker (*2104*) 1939 discussed a number of types of aerosols and considered their relative values. Methods of producing aerosols, their effective particle size range as well as their toxic effects, were discussed in 1940 by Twort, Baker, Finn, and Powell (*2108*). According to Baker and Twort (*2093*) 1941, volatilized or nebulized aerosols are usually more effective in a high humidity. There is an irregular variation in effectiveness on different strains of the organism to be acted upon and with the various bactericides and methods of producing the mist.

In an experiment carried out on the efficacy of triethylene glycol for air sterilization, Bigg, Jennings, and Olson (*2094*) 1944 treated living quarters with this substance. The experiment was conducted on 3 groups of 640 men. The concentration of triethylene glycol in the air varied from 0.0025 to 0.004 mgm. per liter of air. In the experimental groups, the incidence of positive throat cultures (hemolytic streptococci) fell sharply. The investigators also reported a reduced incidence of colds, catarrhal fever, measles, mumps, influenza, scarlet fever, rheumatic fever, acute tonsillitis, chickenpox, acute sinusitis, and pneumonia. In the 6-week period during which the experiments were carried out, there was an over-all

reduction in the sickness rate of 12 percent. During the first 17 days of experiment, the incidence of sickness was reduced by 64 percent in comparison with control conditions.

DeOme and the U. S. Navy Medical Research Unit No. 1, Berkeley, Calif. (*2098*) 1944 reported that the germicidal power of a given concentration of triethylene glycol vapor decreases as the temperature increases from 28° up to 37° C. and as the relative humidity deviates from approximately 45 percent. At relative humidities of 15 and 80 percent, triethylene glycol vapor was reported to have no appreciable germicidal power. The concentration of propylene glycol required to produce a given effect was found to be approximately 100 times that required for triethylene glycol. In 1944, Puck, Wise, and Robertson (*2102*) described a device for automatically controlling the concentration of glycol vapors in the air. It is important that the concentration of glycol be maintained at a level between the minimum bactericidal point and the fog-causing saturation level. Although the fog is nontoxic, it is psychologically undesirable. The method described by the authors is based on the fact that when the vapor condenses on a cooled surface, there is interference with the transmission of a ray of light. This fluctuation in illumination intensity acts on a photoelectric cell by which the glycol vaporizer is turned on or off.

In 1944, Schneiter, Hollaender, Caminita, Kolb, Fraser, Du Buy, Neal, and Rosenblum (*2106*) published a report on the effectiveness of ultraviolet irradiation of upper air for the control of bacterial air contamination in sleeping quarters. Experiments were carried out in 4 dormitories at the National Training School for Boys, Washington, D. C. Ventilation depended on windows only. A total of 90,000 milliwatts of 2,537 Å radiation was provided in 2 dormitories for 18 months. The 2 other dormitories were used as controls. Bacterial counts were made in air samples collected several times each day in all dormitories. Every month, nasal swab cultures were taken from 10 boys in each of the 4 dormitories. During the major portion of this investigation, the predominating microorganisms encountered in nasal swab cultures, air samples, and floor-dust samples were staphylococci. However, in a 5-month period from June to October 1942, the predominant organisms were streptococci. Ultraviolet irradiation effected a reduction in the numbers of viable organisms in the air and, to a lesser degree, in floor-dust. However, the incidence of airborne diseases showed no significant difference under the conditions of this experiment.

Glycol vapors have an important bactericidal effect, according to Hamburger, Robertson, and Puck (*2099*) 1945. These authors discussed factors influencing the efficacy of glycol vapors and apparatus for the dispersion and the regulation of the glycol content of the air. Studies of the toxicity of glycol vapors were also reported. Monkeys and rats lived for 1 year or more in an atmosphere containing propylene and triethylene glycol without suffering any ill effects.

The reader should consult a summary of a 3-year study of the clinical applications of the disinfection of air by glycol vapors published in 1945 by Harris and Stokes (*2100*). A paper dealing with methods of bacterial air analysis by Ruehle (*2105*) 1915 and two further papers on air sterilization by Brunet (*2095*) 1924 and Marino (*2101*) 1929 may be consulted.

The question of the value of aerosols for disinfection of air in submarines cannot be answered without more experimental data. Under conditions of operation in World War II, submarine personnel have been remarkably free from airborne infections. Upper respiratory infections have constituted a problem chiefly during a period of approximately 2 weeks after a submarine has called at a port. Colds and catarrhal fever tend to go the rounds of the crew and there is usually no more difficulty from this cause during the rest of the patrol. Recent studies indicate that with propylene glycol vapor, there is danger of electrical short-circuiting in submarines and also a fire hazard.

2093. Baker, A. H. and C. C. Twort. The effect of humidity of air on the disinfection capacity of mechanically atomized and heat-volatilized germicidal aerosols *J. Hyg., Camb.*, 1941, *41:* 117–130. [P, R]

2094. Bigg, E., B. H. Jennings, and F. C. W. Olson. Epidemiologic observations on the use of glycol vapors for air sterilization. *Proc. cent. Soc. clin. Res.*, 1944, *17:* 38–39. [P]

2095. Brunet, F. Assainissement des atmosphères confinées des navires de guerre. *J. Méd. Bordeaux*, 1924, *96:* 599–601.

2096. Cambier, R. Assainissement et stérilisation de l'air confiné. *Bull. Acad. Méd. Paris*, 1929, *102:* 13–15. [P]

2097. d'Arsonval, [ ], [ ] Bordas, and [ ] Touplain. La purification électrique de l'air. *C. R. Acad. Sci., Paris*, 1920, *170:* 636–638. [P]

2098. DeOme, K. B. and U. S. Navy Medical Research Unit No. 1, Berkeley, California. The effect of temperature, humidity, and glycol vapor on the viability of air-borne bacteria. *Amer. J. Hyg.*, 1944, *40:* 239–250. [P]

2099. Hamburger, M., Jr., O. H. Robertson, and T. T. Puck. The present status of glycol vapors in air sterilization. *Amer. J. med. Sci.*, 1945, *209:* 162–166. [P]

2100. Harris, T. N. and J. Stokes, Jr. Summary of a 3-year study of the clinical applications of the disinfection of air by glycol vapors. *Amer. J. med. Sci.*, 1945, *209:* 152–156. [P]

2101. Marino, V. L'ozono nella epurazione batterica dell'aria di ambienti confinati. *Ann. Igiene (sper.)*, 1929, *39:* 350–357.

2102. Puck, T. T., H. Wise, and O. H. Robertson. A device for automatically controlling the concentration of glycol vapors in the air. *J. exp. Med.*, 1944, *80:* 377–381. [P]

2103. Pulvertaft, R. J. V., G. C. Lemon, and J. W. Walker. Atmospheric and surface sterilisation by aerosols. *Lancet*, 1939, *1:* 443–446. [P, R]

2104. Pulvertaft, R. J. V. and J. W. Walker. The control of air-borne bacteria and fungus spores by means of aerosols. *J. Hyg., Camb.*, 1939, *39:* 696–704. [P, R]

2105. Ruehle, G. L. A. Recent methods of bacterial air analysis. *Amer. J. publ. Hlth*, 1915, *5:* 603–607. [P, R]

2106. Schneiter, R., A. Hollaender, B. H. Caminita, R. W. Kolb, H. F. Fraser, H. G. Du Buy, P. A. Neal, and H. B. Rosenblum. Effectiveness of ultraviolet irradiation of upper air for the control of bacterial air contamination in sleeping quarters. Preliminary report. *Amer. J. Hyg.*, 1944, *40:* 136–153. [P, M]

2107. Trillat, A. and [ ] Fouassier. Influence de la radioactivité de l'air sur les gouttelettes microbiennes de l'atmosphère. *C. R. Acad. Sci., Paris*, 1914, *159:* 817–820. [P]

2108. Twort, C. C., A. H. Baker, S. R. Finn, and E. O. Fowell. The disinfection of closed atmospheres with germicidal aerosols. *J. Hyg., Camb.*, 1940, *40:* 253–344. [R]

2109. Van Rensselaer, H. Impure air, and ventilation of private dwellings. *Trans. N. Y. med. Ass.*, 1891, *8:* 391–418.

2110. Wells, W. F. Air-borne infection and sanitary air control. *J. industr. Hyg.*, 1935, *17:* 253–257. [P]

2111. Wells, W. F. Circulation in sanitary ventilation by bactericidal irradiation of air. *J. Franklin Inst.*, 1945, *240:* 379–395. [P, M]

2112. Wells, W. F. and H. W. Brown. Recovery of influenza virus suspended in air and its destruction by ultraviolet radiation. *Amer. J. Hyg.*, 1936, *24:* 407–413. [P]

2113. Wells, W. F. and G. M. Fair. Viability of B. coli exposed to ultra-violet radiation in air. *Science*, 1935, *82:* 280–281. [P]

2114. Wells, W. F. and M. W. Wells. Air-borne infection. *J. Amer. med. Ass.*, 1936, *107:* 1698–1703; 1805–1809. [P]

2115. Wells, W. F. and M. W. Wells. Measurement of sanitary ventilation. *Amer. J. publ. Hlth*, 1938, *28*(1): 343–350. [P, R]

V. SUBMARINE ESCAPE "LUNG"; OTHER RESPIRATORS

Escape from a disabled submarine is possible without the use of any apparatus whatever and such free escapes from depths of 100 ft. have been repeatedly accomplished in the escape training tower at the U. S. Submarine Base, New London, Conn. It is necessary to exhale as the ascent is made so that the expanding air in the lungs may be liberated from the body. To aid personnel in effecting safe escapes to the surface, the escape "lung" has been devised. This consists essentially of an airtight, watertight bag which can be filled with oxygen or air and a canister for absorbing carbon dioxide. There is a mouthpiece and a two-way valve for inhalation and exhalation. A flutter valve at the bottom of the bag is designed to release excess pressure as the individual ascends. A nose clip is used. Mankin (*2125*) 1930 has described the early history of the escape "lung" and the test escapes carried out with it. Reference should be made also to a report by Brown (*2116*) 1931–32 on individual escape from submarines using the "lung." The device was developed chiefly by Momson, Tibbels, and Hobson. Work on the "lung" was greatly stimulated by the loss of the S-4, sunk in approximately 100 ft. of water off

Cape Cod by a collision in 1926. Since submarines may sink to great depths without injury to the hull, and personnel may remain alive, escape apparatus and training are of utmost importance. The "lung" also has a value on reaching the surface in maintaining the individual afloat. If an escape is to be made from a compartment not provided with an escape lock, the compartment must be flooded to equalize the pressure between the inside of the compartment and the water outside. The flooding of the compartment requires approximately 10 to 20 minutes. The "lung" is then charged with oxygen but breathing from the bag is not commenced until a few minutes before emergence. When the pressure is equalized, the escape hatch is thrown open and a line passed up. The men duck under the water and under the skirt and slide up the line at a rate of 50 ft. per minute. The hazard of caisson disease is not usually great because of the shortness of the time to which the individual is exposed to raised atmospheric pressure. However, rescue ships are provided with compression chambers to treat survivors if necessary. At the time of Brown's report, simulated escapes had been made with the "lung" at the Experimental Diving Unit, Navy Yard, Washington, D. C. in a high pressure diving tank from an equivalent depth of 374 ft. and actual escapes from submarines had been accomplished from a depth of 260 ft.

Brown described the escape training tower at the U. S. Submarine Base, New London, Conn. This tower is approximately 136 ft. high and 18 ft. in diameter and contains a column of water 100 ft. deep. Escape locks are provided at levels of 18 ft. and at 50 ft. and a simulated submarine compartment is provided at 100 ft. All submarine personnel are required to undergo training in the escape tower, escape from 18 ft. being required and escape from 50 and 100 ft. being voluntary. The principal danger in effecting an escape with the "lung" lies in the tendency of some untrained personnel to hold the breath during escape. This produces severe trauma which may be rapidly fatal. The literature on these accidents is discussed on page 223.

For further reports on the mechanism of respiration in relation to the escape "lung," papers by Davies, Haldane, and Priestley (*2119*) 1919–20; Hörnicke and Bruns (*2120*) 1927; and Brunton (*2117*) 1929 may be consulted.

Other respirators of significance in subaqueous operations are referred to in reports by the following authors: Macintosh (*2124*) 1922, Cornish (*2118*) 1933, Lambertsen (*2123*) 1941, and Schrenk (*2126*) 1940.

2116. Brown, E. W. Individual escape from submarines. *Yale sci. Mag.*, 1931–32, *6*(3): 9–10; 29–31. [R]

2117. Brunton, C. E. The nervous regulation of respiration. Response of the human subject to interruption of the air supply. *J. Physiol.*, 1929, *67:* 191–198.

2118. Cornish, R. E. Improving underwater vision of lifeguards and naked divers. *J. opt. Soc. Amer.*, 1933, *23:* 430.

2119. Davies, H. W., J. S. Haldane, and J. G. Priestley. The response to respiratory resistance. *J. Physiol.*, 1919–20, *53:* 60–69. [P]

2120. Hörnicke, E. and O. Bruns. Atemphysiologische Beobachtungen beim Gebrauch von Industrie-Schutzmasken. I. Mitteilung. Die Bedeutung des Individuums für die Verwendbarkeit der Maske. *Z. ges. exp. Med.*, 1927, *56:* 98–117.

2121. Jenkinson, S. Submarine salvage. The air in a submerged submarine: means of exit when submerged: and disabilities of the survivors. *Brit. J. Surg.*, 1939–40, *27:* 767–780. [R]

2122. Johnston, J. The Davis submarine escape apparatus. *J. R. nav. med. Serv.*, 1931, *17:* 12–18. [R]

2123. Lambertsen, C. J. A diving apparatus for life saving work. *J. Amer. med. Ass.*, 1941, *116:* 1387–1389.

2124. Macintosh, G. D. A Japanese diving appliance. *J. R. nav. med. Serv.*, 1922, *8:* 300–301.

2125. Mankin, G. H. Individual submarine escape. *Nav. med. Bull., Wash.*, 1930, *28:* 18–28. [R]

2126. Schrenk, H. H. Testing respiratory protective equipment for approval. *Inform. Circ. U. S. Bur. Min.*, 1940, no. 7130, 1–9. [R]

2127. Severin, G. Räddning från sjunken undervattenbåt. En översikt med särskild hänsyn till de höga tryckens verkningar på organismen. *Nord. Med., Stockholm*, 1940, *8:* 1685–1694. [R]

VI. DIVING BELLS AND SUBMARINE ESCAPE CHAMBERS

For accounts of the development of diving bells and escape chambers, reference should be made to papers on the history of diving

(p. 5). Further information may be obtained from a short note by Richardson (*2128*) 1880.

2128. Richardson, [ ]. Fluess's new diving apparatus, and on living in irrespirable air. *Lancet,* 1880, *1:* 957–958. [R]

VII. SUBMARINE DISASTERS AND SALVAGE

In flooding of mines, air will be driven into the upper headings and stalls under a pressure equal to the height of the column of water in the mine. Davies (*2130*) in 1877 described such a catastrophe in which five men were entombed in a stall under a pressure of 25 lb. per sq. in. Four of the workers were rescued and one died.

Descriptions of submarine disasters and salvage operations are for the most part limited to the unpublished, classified literature. However, a certain number of references are found in the open literature. French (*2131*) 1916 described diving operations in connection with the salvage of the F–4. This report includes a discussion of the air supply of the diver's helmet and the physical condition of the divers engaged in the work. One case of caisson disease was reported.

Seaman (*2135*) 1916 reported on the recovery, identification, and disposition of remains of the crew of the F–4. This submarine was lost on 25 March 1915 1½ miles outside Honolulu Harbor at a depth of 305 ft. The wreck was shifted to a depth of 40 ft. and was raised the following August. The remains of the crew were in states of decomposition varying from complete obliteration to a fair state of preservation. There was no way of determining the cause of the disaster or the death of the men. The interior of the vessel was a complete wreck. Four bodies were found amidships while the remainder were in the after compartment or the engine room. Nine days were required to locate all human remains. Of 17 bodies, only 4 could be positively identified. Only 6 skulls were found, the others having been washed away. The skulls were denuded of all tissue except the eyeballs. The maxillae were disarticulated and 5 of the skulls showed one or more fractures. The fatty substance on the bones in the middle compartment had been converted into adipocere. Where the feet were covered by shoes, flesh was well preserved, the shoes themselves being in good condition. Identification of two bodies was made from dental records; one body was identified from a notebook and a fourth from articles in the pockets of the clothing still adhering to the body. The remains were placed in metal caskets and returned to the United States. As aids to identification, Seaman suggested attention to accuracy of dental records, dog tags worn on the ankle, and initials cut into the heels of the shoes.

The salvage of the Italian dreadnought *Leonardo da Vinci* was described in 1921 by Guidoni (*2132*). This vessel sank in 1916 after an explosion in a magazine and settled at a depth of 6 fathoms. Raising the ship was accomplished by filling its compartments with compressed air. All superstructures were cut off and leaks mended. The hull was then filled with compressed air and floated to a dry dock at Taranto. The guns, etc., were recovered from the bottom of the sea by divers.

One of the most remarkable treasure salvage operations in the history of diving is the recovery of the gold bullion from the *Laurentic* from 1917 to 1924. These operations were described by Damant (*2129*) in 1926. The *Laurentic* was a 15,000-ton Atlantic liner converted into an armed cruiser during World War I. Early in 1917, the *Laurentic* sailed from Liverpool with £5,000,000 of gold bullion. Before clearing the Irish Coast, the vessel was sunk by enemy mines with great loss of life. The wreck was located at a depth of 20 fathoms exposed to the full run of the north Atlantic weather from the north and west. Divers located the ship listing about 60° from the vertical on her port bilge. Six weeks after the sinking, divers blew open an entry port half way down the ship's side 60 ft. from the surface and reached the second-class baggage room where the gold was stored. Diver E. C. Miller brought out 4 boxes of gold each worth £8,000. After the fourth box had been

salvaged, a wind came up, and a gale blew for a week. When diving was again possible, the entry port lay at a depth of 103 ft. and the passage to the baggage room had collapsed. This was forced clear by explosives and a tunnel established. The baggage room was finally reached at a depth of 120 ft. but the room was empty and the floor gaping with large rents. Salvage operations then consisted in bringing up loose bars from the sea bottom, a procedure which required 7 seasons of work.

On one occasion, a German mine was exploded 2 miles away by a mine sweeper and on another, an explosion occurred 6 miles away. The divers received violent blows but were not injured. Damant commented on the problems of air supply to divers and the work of the Admiralty Committee on Underwater Diving, with particular reference to prevention and treatment of decompression sickness. During the entire salvage operation, there were 31 cases of decompression sickness out of approximately 5,000 dives, the majority of which reached pressures of 53 to 59 lb. per sq. in. A recompression chamber was available for the treatment of compressed air illness. The air supply for the divers was provided by a steam air compressor capable of delivering 100 cu. ft. per min. This maintained a pressure in a large reservoir at 100 lb. per sq. in. From this reservoir, there were 4 ducts, 1 to the recompression chamber and 3 to the divers. There was 1 case of a diver being "blown up." This diver, Light, was working with his head down and his dress became filled with air. He was blown up to a depth of about 40 ft. His airpipe was tied with a lanyard to the wreck so that he was held upside down in midwater. Another diver, Blanchard, climbing down Light's airpipe, cut the lanyard fastening it to the wreck and both divers were blown instantly to the surface. Light was put in the decompression chamber and recovered. Damant states that it would have been better policy to have tried to capsize Light by pulling on his feet.

The entire *Laurentic* salvage operation was conducted without the loss of a single life. Three-thousand two-hundred and eleven bars of gold went down with the wreck and 3,186 were recovered at a cost of 2 to 3 percent of the value of the gold salvaged.

For a further account of the problems facing divers operating from a salvage ship, reference should be made to a book by Scott (*2134*) describing 3 seasons' work with the Italian salvage ship *Artiglio*, belonging to the Marine Salvage Company, commonly known as the "Sarima" of Genoa, Italy. In 1929 and 1930, the *Artiglio* sought and found the wreck of the P & O liner, *Egypt*, sunk in 400 ft. of water 30 miles off the coast of Brittany. The divers of the *Artiglio* successfully salvaged £1,000,000 worth of gold and silver from this wreck. In December, 1930 the *Artiglio* was destroyed by the explosion of a cargo of munitions in a wreck upon which the crew of the *Artiglio* was working. Scott's book describes the articulated, rigid, self-contained diving shells (Neufeldt and Kuhnke type) used in the deep-diving operations and may be profitably consulted for an account of the daily life of divers.

2129. Damant, G. C. C. Notes on the "Laurentic" salvage operations and the prevention of compressed air illness. *J. Hyg., Camb.*, 1926, *25:* 26–49, pls. 1–5. [R]

2130. Davies, H. N. The recent catastrophe at Tynewydd Colliery, near Pont-Y-Pridd. *Brit. med. J.*, 1877, *1:* 580–582. [P]

2131. French, G. R. W. Diving operations in connection with the salvage of the U. S. S. "F–4." *Nav. med. Bull., Wash.*, 1916, *10:* 74–91. [R]

2132. Guidoni, A. The salvage of the *Leonardo da Vinci*. *Proc. U. S. nav. Inst.*, 1921, pp. 1689–1696. [R]

2133. Mankin, G. H. Medical aspects of the salvage of the U. S. submarine "S–4". *Nav. med. Bull., Wash.*, 1928, *26:* 557–566. [R]

2134. Scott, David. *Seventy fathoms deep, with the divers of the salvage ship Artiglio.* London, Faber & Faber Ltd., 288 pp. [R]

2135. Seaman, W. Report on the recovery, identification, and disposition of the remains of the crew of the "F–4". *Nav. med. Bull., Wash.*, 1916, *10:* 91–96. [R]

2136. Anon. Life-saving service without recognition. *J. Amer. med. Ass.*, 1940, *115:* 2000–2001.

2137. Anon. Navy divers clear out captured harbors. Work ranges from destroying vessels to salvaging them. *Bur. nav. Pers. Inform. Bull.*, 1944, No. 330, pp. 26–29.

VIII. BATHYSPHERES

Using a steel observation chamber 57.3 inches in outside diameter and constructed of

steel 1.5 inches thick, Beebe and Barton descended on June 11, 1930 to a depth of 1,426 ft. In such observation chambers, the pressure is maintained at 1 atmosphere and oxygen is supplied in compressed air tanks. Carbon dioxide is absorbed by carbon dioxide absorbents. Such chambers are of use in making deep-sea observations for scientific purposes and to locate and identify wrecks. Beebe's bathysphere was referred to by Osborn (*2138*) 1930.

2138. Osborn, H. F. A new method of deep sea observation at first hand. *Science*, 1930, *72:* 27–28.

2139. Anon. Deep sea investigations by submarine observation chamber. *Nature, Lond.*, 1930, *126:* 220.

IX. SUBMERSIBLE DECOMPRESSION CHAMBERS

Information on the Davis submersible decompression chamber may be found in papers by Hill (*2140*) 1930 and Thomson (*2141*) 1935. The chamber was equipped to hold two men and could withstand a pressure of 100 lb. per sq. in. It was lowered to a depth of 60 ft., at which level the diver entered and began to breathe oxygen. The chamber could be hauled onto the deck for decompression. While such a device was found to possess advantages, it has been determined that divers can be brought rapidly to the surface if necessary, placed under pressure in a recompression chamber and then slowly decompressed without harm.

2140. Hill, L. Diving. *Not. Proc. roy. Instn.*, 1930, *26*(2): 184–192. [R]

2141. Thomson, W. A. R. The physiology of deep-sea diving. *Brit. med. J.*, 1935, *2:* 208–210. [R]

X. DIVING DRESS

The reader will find allusions to diving dress in the section on history of diving (p. 5). For further reference to early diving suits, a paper by du Mesnil (*2146*) published in 1868 may be consulted. This paper described a suit devised by Cabirol which was supplied with air under pressure from a pump at the surface. A description was also given of the Rouquayrol-Denayrouse apparatus which consisted of a surface air pump plus a reservoir on the diver's back by which air was furnished to the diver at a pressure which varied with the depth at which the diver was working.

A description of the Fleuss self-contained diving apparatus was given in 1879-80 by Richardson (*2148*). With this equipment, the inventor remained at a depth of 12 ft. for 1 hour, carrying out movements and manual work.

Diving apparatus was described by Khrabrostin (*2145*) in 1888. Spectacles to aid vision in divers without apparatus were described by Stevenson (*2149*) in 1891. Lambertson (*2123*) 1941 referred to a self-contained diving apparatus for lifesaving work. With this apparatus, divers could remain submerged for 18 to 25 minutes at depths up to 60 ft.

Modern diving devices were described by Damant (*2143*) in 1931 and other references to diving apparatus are to be found in reports by the following authors: Fiorito (*2144*) 1913, Chastang (*2142*) 1920, Zburzhinsky and Annin (*2150*) 1931, and Moschini (*2147*) 1934.

2142. Chastang, [ ]. Le scaphandre autonome. *Arch. Méd. Pharm. nav.*, 1920, *109:* 290–295. [P]

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XI. PREVENTION AND TREATMENT OF DECOMPRESSION SICKNESS

A. HOURS OF LABOR, COMPRESSION AND DECOMPRESSION TIMES, AND RECOMPRESSION TREATMENT IN CAISSON AND TUNNEL WORKERS

1. EARLY STUDIES

Initiation of ways to prevent or treat decompression sickness coincides with the beginning of the use of raised atmospheric pressures in subaqueous engineering operations. It was early recognized that the incidence of caisson disease is in some way related to hours of labor under increased pressure and particularly to the rate at which the workers are decompressed to normal pressure.

Pol and Watelle (*75*) 1854 were the first to make detailed observations of caisson disease and to give specific attention to regulations governing compression and decompression times and length of working shifts under pressure in the caisson. In their report, they stated that the entire working personnel of 64 men of the mining operations at Douchy were divided into gangs of 6 or 7 each laboring alternately in 4-hour shifts twice during each 24 hours. One-quarter hour was spent in compressing workmen in the lock from atmospheric pressure to the pressure within the caisson. At first, the decompression time was one-fourth hour; however, as the caisson sank deeper and the pressure within the working chamber was increased, the "locking-out" time was raised to one-half hour. The maximum pressure attained in the caisson during the operation was 4.5 atmospheres (absolute).

About 1856, the new plenum method of sinking a shaft through water or water-bearing sands was used at the coal mines at Eischweiler near Aix-les-Chapelles. The mines at Eischweiler were reopened in 1859 using pressures up to 3.5 atmospheres (absolute). von Vivenot (*2638*) 1860 reported that the men worked 6-hour shifts. There was excessive sweating followed by thirst on leaving the mine, and impairment of the appetite was a common complaint.

In 1860, an account of the medical problems of workmen excavating in caissons in the construction of a bridge over the Rhine at Strassbourg was given by François (*1169*) 1860. In this construction, 14 caissons, each 7 m. long, 5.8 m. wide and 3.5 m. high, were used. The locks were 2 m. in diameter and 4 m. high. On "locking in," men experienced progressive impairment of hearing and there was some rise of the temperature within the lock. On leaving the caisson, workmen sometimes complained of pain in the ears and there were commonly complaints of muscle and joint pains as well as itching of the skin, hemoptysis, and nose bleed. In some instances, these symptoms came on soon after leaving the caisson while in other cases the attack was deferred for some hours. Sometimes, the men on leaving the lock fell almost as if struck by lightning. In this particular construction, the attacks usually passed off quickly and only one fatality was recorded. The decompression times used were as follows:

Barometric pressure	Times of decompression
Atmospheres (absolute)	*Minutes*
1.25 to 1.50	4 to 5
2.0	5 to 7
2.5	10
3.0	12

Pravaz (*2194*) 1861 stated that in the compressed air chambers in his pneumatotherapeutic institute there had never been any accidents although they had functioned 6 days a week for 4 to 5 hours a day for 21 years. This is not surprising, since the chambers in question operated at relatively low pressures and were used solely for therapeutic purposes. (See p. 304.) Pravaz believed that accidents to workers in caissons were caused by liberation, on rapid decompression, of gases dissolved in the blood or tissues. These gas bubbles were thought to lacerate tissues and blood vessels. Pravaz suggested that decompression times of one-half to three-fourths hour be used for lowering pressures within the caisson from levels of 2 to 3 atmospheres (absolute) down to normal.

In 1863, Foley (*202*) published a monograph reporting observations on the effects of

compressed air on workers employed in sinking piers for a bridge at Argenteuil. As the pressure rose on "locking in," the ears were affected and there were sometimes darting pains through the forehead, nasal cavities, and jaw. The voice acquired a metallic tone and whistling became difficult or impossible. Workmen sometimes complained of stammering. Sense of taste, smell, touch, and hot and cold were said to be less acute. The pulse was small and thready and the venous blood bright red. Workers often noticed increased appetite, particularly at first. During the work period in the caisson, while the pressure remained stationary, symptoms disappeared. However, on "locking out," there were ringing in the ears, loss of taste and smell, a prickling sense of warmth in the nostrils, and sometimes bleeding at the nose. At first, laborers in compressed air at Argenteuil worked two 4-hour shifts during each 24 hours. Later, it was necessary to diminish the hours of work. During "locking out," the workmen were decompressed at a rate of 1 minute for each atmosphere. A longer time of decompression, namely, a rate of 10 minutes per atmosphere, was recommended by Barella (*1046*) 1868.

Numbers of observers considered the provisions of an adequate decompression time of primary importance. Jaminet (see *2204*) in 1871 advised against too sudden changes from normal to condensed air in the case of workers at the St. Louis bridge over the Mississippi. In this gigantic construction operation, caissons were sunk to a maximum depth of 115 ft. below the level of the river surface. Seventy-eight cases of decompression sickness were reported, including eight fatalities. In pressures up to 50 lb. per sq. in. (gauge), the men worked three 2-hour shifts in each 24 hours with 2-hour rest periods in between. Jaminet ordered that workers be "locked in" at a rate not greater than 1 minute for every 3 lb. per sq. in. of pressure increase. Contrary to modern practice, he considered quick decompression the safest, and workers at the St. Louis Bridge were "locked out" at a rate of 1 minute for every 6 lb. per sq. in. of pressure fall.

In the construction of the Brooklyn Bridge in New York (see Smith (*76*) 1873), the maximum pressure used in the caisson on the New York side was 36 lb. per sq. in. The caissons had a horizontal dimension 102 ft. by 172 ft. and on the New York side, solid foundation was reached at a depth of 78 ft. below the high-water mark. By increasing the number of compressors by which air was supplied, the concentration of carbon dioxide within the caissons was kept below a level of 0.33 percent. A flow of 150,000 cu. ft. of air per hour was considered a minimal requirement. Fifty to one hundred twenty-five workers were employed in the caisson by day and 15 to 30 by night. At first, each man worked 2 shifts of 4 hours each with an interval of 2 hours between the shifts. Finally, the working periods were reduced to 2 shifts of 2 hours, each separated by an interval of 4 hours. Workers were cautioned not to enter the caisson on an empty stomach and a meat diet was advised. The importance of warm clothing on "locking out" was stressed.

Workers were told to exercise as little as possible during the first hour following emergence. Other rules included sparing use of intoxicants, 8 hours of sleep each night, and regular bowel habits. Workers were cautioned not to enter the caisson if not well and all cases of illness of whatever sort were to be reported to the plant physician. Regarding treatment, Smith gave anodynes for the relief of pain. One-half grain of morphine, followed by an additional one-fourth grain each succeeding hour, was recommended. In some cases, atropine was injected hypodermically at the site of pain. Smith also claimed considerable success in the use of ergot, which was usually administered by mouth in the form of the fluid extract.

Smith was apparently the first to suggest the use of a specially constructed medical or "hospital" lock in which cases of decompression sickness could be treated by recompression and subsequent slow decompression. Caisson workers, from the inception of the compressed air system of subaqueous construction work, have relieved the "bends" by reexposure to the raised atmospheric pressures within the caisson.

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Smith's medical lock was an iron chamber 9 ft. long and 3½ ft. in diameter. It was equipped with a glass port and adequate ventilation was provided for. The procedure was to put the patient into the chamber, raise the pressure to equal that at which the patient had been previously working and when the pain was relieved, to reduce the pressure gradually. Often decompression lasted for several hours.

In 1878, Wagner (*2213*) published the following recommendations:

(a) Times of compression:
- Compression to plus 0.5 atmospheres (7.3 lb.) in 5 minutes.
- Compression to plus 1.0 atmospheres (14.7 lb.) in 8 minutes.
- Compression to plus 1.5 atmospheres (22.0 lb.) in 12 minutes.
- Compression to plus 2.0 atmospheres (29.4 lb.) in 15 minutes.
- Compression to plus 2.5 atmospheres (36.7 lb.) in 20 minutes.
- Compression to plus 3.0 atmospheres (44.1 lb.) in 25 minutes.

(b) Duration of work:
- At a pressure of plus 1 atmosphere (14.7 lb.), duration of work should be 1 shift of 8 hours in 24 hours.
- At a pressure of plus 2 atmospheres (29.4 lb.), duration of work should be 1 shift of 6 hours in 24 hours.
- At a pressure of plus 3 atmospheres (44.1 lb.), duration of work should be 1 shift of 4 hours in 24 hours.

(c) Times of decompression (uniform rate):
- From plus 0.5 atmospheres, decompression in 5 minutes.
- From plus 1.0 atmospheres, decompression in 10 minutes.
- From plus 1.5 atmospheres, decompression in 15 minutes.
- From plus 2.0 atmospheres, decompression in 20 minutes.
- From plus 2.5 atmospheres, decompression in 30 minutes.
- From plus 3.0 atmospheres, decompression in 40 minutes.

Interest in prevention of caisson accidents was shown by Triger, as Moeller (*2185*) 1881 indicated. Moeller stated that in 1862, there were two deaths among workers employed in constructing a viaduct at Lorient, France. At the construction of a bridge at Bayonne in 1862 the maximum barometric pressure was 4 atmospheres (absolute). The engineer was stricken with unconsciousness followed by paralysis on exit from the caisson after a decompression time of only 4 to 5 minutes. The paralysis persisted for 2 years. This case has been reported by Limousin (*1258*) 1863 who considered the condition to be due to a hemorrhage in the spinal cord.

At about this time, an explosion of a caisson took place and two workmen were killed. It was impossible to establish beyond doubt whether the sudden decompression was the cause of death or not. Several other workers present in the chamber were unaffected by the explosion. In 1865, there was an explosion of a caisson used in the construction of a bridge at Chalonnes. Two workers were killed in this accident. Autopsies were performed under conditions unsatisfactory for determining the cause of death. Motivated by these accidents, Triger (see *2185*) sent to the ministry of public works a *memoire* prepared by himself and others. It was stated that accidents in caissons could be prevented by slow decompression and by the use of warm clothing. Triger considered a period of 7 minutes adequate for total decompression.

Moeller (*2185*) 1881 called attention to rules governing the avoidance of alcoholic beverages, not entering the caisson if not feeling well, and avoiding violent body exercises after exit from the caisson. He believed that the proper treatment of caisson disease consisted in rapid recompression followed by slow decompression. He considered that breathing pure oxygen might provoke expulsion of nitrogen from the body. Moeller recommended that above pressures of 5 atmospheres it would be well to use air mixtures with a lower oxygen percentage than normal.

In a thesis published by Chabaud (*2156*) in 1883, the author suggested a period of ½ to 1 minute for decompression from 3 to 1 atmospheres (absolute). It was Chabaud's opinion that working two 6-hour shifts a day was excessive and that single work periods should not exceed 4 or 5 hours in duration. He considered that workmen would not be harmed by two such shifts in 24 hours. In general, the earlier investigators recom-

mended longer shifts and allowed more rapid decompression than present practice permits. Moreover, the physiological limits of tolerance of compression were estimated to be much higher.

In 1896, Drasche (*2163*) published the following table giving compression time, hours of work, and decompression times:

Air Pressure atmosphere (absolute)	Compression time (Minutes)	Duration of actual work		Number of shifts in 24 hours	Decompression time (Minutes)
		Hr.	Min.		
1 to 2	5	5	50	2 shifts of 6 hours	5
Up to 2.75	8	5	42	2 shifts of 6 hours	10
Up to 3	10	3	35	2 shifts of 4 hours	15
Up to 3.5	13	3	22	2 shifts of 4 hours	25
Up to 4	15	1	26	2 shifts of 3 hours	35
Up to 4.5	20	1	55	2 shifts of 3 hours	45

Heller, Mager, and von Schrötter (*2172*) 1899 made a careful study of conditions prevailing in workers in a tunnel under the Danube at Nussdorf. In this operation, there was a high incidence of compressed air illness and two deaths. In order to lower the sickness rate in such workers, Heller, Mager, and von Schrötter recommended that "locking in" be carried out at a rate of 1 minute for each one-tenth of an atmosphere (1.5 lb.). This rule was particularly to be observed for newcomers. For old hands, this time could be decreased but the following times were considered a minimum:

For compression to plus 0.5 atmospheres (7.3 lb.), never less than 5 minutes.

For compression to plus 1.5 atmospheres (22 lb.), never less than 10 minutes.

For compression to plus 2.5 atmospheres (37 lb.), never less than 15 minutes.

For compression to plus 3.5 atmospheres (51 lb.), never less than 20 minutes.

For compression to plus 5.0 atmospheres (74 lb.), never less than 30 minutes.

It was considered permissible for workers to remain in compressed air up to 8 hours. Two 4-hour shifts or one 6- to 8-hour shift in every 24 hours were recommended. Decompression was to be carried out at a rate not exceeding 0.1 atmosphere (1.5 lb.) for every 2 minutes. It was considered by Heller, Mager, and von Schrötter that decompression should be uniform. The authors recommended at least 0.7 cubic meters of air space per person in the decompression lock. In operations where the working pressure was higher than 2.5 atmospheres (absolute), it was recommended that a recompression chamber be available. In cases of caisson disease, the patient was to be placed immediately in the recompression chamber and taken to the pressure level at which he had previously been working. He was to remain at this pressure level until all symptoms had disappeared and then be decompressed at a rate of 0.1 atmospheres every 3 minutes. Heller, Mager, and von Schrötter believed that with proper precautions, workers could tolerate pressures up to 5 atmospheres. Only men between the ages of 20 to 50 were accepted and disease of the lungs, cardiovascular system, or the ears were considered disqualifying. The rules excluded from caisson work those who were intemperate in the use of alcohol.

In the caisson operations reported by Oliver (*2188*) 1899–1900, a decompression rate of at least 1 minute for every 3 lb. per sq. in. of pressure was recommended. With this schedule, serious cases of caisson disease occurred. For example, one worker with 20 years' experience had been working at levels of 77 ft. below the water level (corresponding to a gauge pressure of 34 lb. per sq. in.). On "locking out," he became giddy, felt numb, and lost consciousness. Twelve hours later, he regained consciousness. The following day, he intended to go to work but again lost consciousness and later suffered from nose bleed, oppression in the chest, pain in the muscles, and loss of power in the legs. Knee jerks were exaggerated but there were no urinary or rectal abnormalities. The patient made a satisfactory recovery.

Further reports of the medical problems involved in caisson work were given by Oliver (*1122*) in 1905–6. Oliver's experience was gained at Newcastle-on-Tyne during the con-

struction of a bridge spanning the Tyne and the building of a high level railroad bridge by the Cleveland Bridge and Engineering Company. To build the foundations for the piers of the latter bridge, excavations were carried out in caissons to a depth of 70 feet. One hundred forty to two hundred workers were employed, only 68 of whom worked under pressure. Thirty to forty men could work in each caisson at once. Each caisson had a cubic capacity of 23,142 cubic feet. The working chamber was 113 feet in length, 35 feet wide and 9 feet 6 inches high and was supplied with 750 cubic feet of air per minute (or 1,320 cubic feet per man per hour). Forty-eight men worked under pressure in all three caissons from start to finish without any symptoms. Twenty-nine men completed work in two caissons for a period of 180 days and maintained good health. Forty-nine men worked for 90 days during the operations in one caisson without symptoms. No applicant over 40 years of age was given employment in the caissons and 4 percent of applicants were rejected. A ventilation of 1,320 cubic feet of air per man per hour was found adequate. However, at the Blackwall Tunnel, Snell (*1191*) 1897 found that a ventilation rate providing 4,000 to 9,000 cubic feet per man per hour was necessary, since the gravelly nature of the soil in this particular operation permitted a freer escape of air than usual.

At the Tyne construction, the hours of labor were long. Men worked from 6:00 a.m. to 8:30 a.m. and then after a rest, from 9:15 a.m. to 1:00 p.m. They then rested an hour and returned to work at 2:00 p.m. and worked until 6:00 p.m. Men were, therefore, working under raised atmospheric pressure for 10¼ hours a day. When the gauge pressure reached as high as 25 lb. per sq. in., 4 hours was the longest time spent continuously in the caisson. "Locking out" was carried out at a rate of 1 minute for every 5 lb. of pressure.

For the most part, decompression schedules in effect at that time in continental European caisson or tunneling operations provided for uniform or nearly uniform rate of reduction of pressure. Such a rate was recommended by Heller, Mager, and von Schrötter (*2172*) 1898. Other rates were somewhat slower at first and became more rapid as decompression proceeded. Haldane (*2167*, *2168*) 1907, at the request of British Admiralty, devised a stage decompression method in which workers were brought rapidly to one-half the absolute pressure, maintained at that level for a short period and then taken by stages to normal pressure. There has been considerable discussion in the literature of the relative merits of the uniform decompression technique and the stage method of Haldane as applied to divers and caisson or tunnel workers. Some of these considerations are referred to on page 267.

For French compression and decompression tables and recommendations governing hours of labor, the reader should consult the papers of Langlois (*2177*, *2178*) published in 1906 and 1907. In his later report, Langlois set forth regulations adopted by a Commission of Industrial Hygiene of the French Ministry of Labor.

In the treatment of compressed air illness in caisson workers, Pelton (*2190*) 1907 stated that the first consideration was recompression of the patient. A hospital lock was described. This was a horizontal cylinder about 25 ft. long and 7 ft. in diameter and was provided with a lock so that entrance and exit of attendants from the main chamber could be effected without altering the pressure to which the patient was subjected. Pelton recommended that the pressure be raised to the height to which the patient had been working and that the pressure then be slowly lowered to normal at a rate of one-half lb. per minute. In some cases, an even slower decompression rate was advisable. Pelton believed it unwise to subject the patient to maximum pressure for longer than 5 to 10 minutes. If pains recurred, the patient was to be recompressed again until pains disappeared and then slowly decompressed as before. Rubbing the affected parts was considered a useful adjunct to recompression and decompression and possible benefit was also suggested from faradic currents, high frequency, or dry heat. Analgesics such as acetanilide (5 grains every 4 hours) were considered

useful. Morphine, according to Pelton, was rarely indicated.

In 1908, Boycott, Damant, and Haldane (*2155*) reported that rapid decompression could be carried out without risk of caisson disease provided atmospheric pressure was not exceeded by more than 18.4 lb. or plus 1.25 atmospheres. According to the Haldane stage method of decompression, the pressure was first rapidly lowered to one-half the absolute working pressure. The pressure was then taken to normal at a rate corresponding to the following table:

Working pressure (pound per sq. in. (gauge))	Number of minutes for each pound of decompression after first rapid stage.		
	After 3 hours' exposure	After second or third 3-hour exposure broken by meal interval.	After 6 hours or more continuous exposure.
18–20	2	3	5
21–24	3	5	7
25–29	5	7	8
30–34	6	7	9
35–39	7	8	9
40–45	7	8	9

These rates were considered by Peters (*2191*) 1908 to be safer than the decompression schedules recommended by the Commission of Industrial Hygiene of the French Ministry of Labor previously referred to. Peters recommended a slow uniform decompression rate of at least 2 minutes for every one-tenth of an atmosphere. For decompression from 7.5 lb. gauge pressure, 1 minute for each one-tenth of an atmosphere (or 1.5 lb.) was sufficient. For decompression from pressures of 7.3 to 22 lb., the time required was recommended to be 5 minutes plus 1½ minutes for each one-tenth of an atmosphere over 7.3 lb. For decompression from pressures between 22 and 44 lb. gauge, the minimum time was to be 20 minutes plus 2 minutes for every one-tenth of an atmosphere over 1.5 atmospheres. For decompression from pressures over 3 atmospheres, the minimum time was given as 50 minutes plus at least 3 minutes for each one-tenth of an atmosphere over 3 atmospheres. According to Peters, any single continuous working period should be limited to 4 hours. It should be noted according to Thomson (*2209*) 1908 that Hersent, as a result of experiments carried out in pressure chambers, believed that compression and decompression should be conducted at a rate of 20 minutes for each 15 lb. of pressure.

From 29 March 1906 to 30 March 1909 Keays was in the employ of S. Pearson and Sons, Contractors. In Keay's report (*2176*) published in 1909, he postulated that the body fluids and tissues probably reach a state of complete equilibrium with nitrogen and other gases in 2 to 3 hours. Therefore, he considered that dividing the shift, provided that the time of working approached the point of body saturation, increased the danger to the worker by doubling the number of decompressions. He believed that 6 hours' continuous work would be preferable to two 3-hour periods. For pressures above 15 lb., the shorter the decompression period the greater the likelihood of decompression sickness. Keays found that recompression treatment relieved pains in 90 percent of cases in which it was carried out. He believed that recompression should be carried out as early as possible to a pressure level equal to the working pressure. The patient should then be decompressed, allowing a time equal in number of minutes to at least twice the number of lbs. pressure. The best results were obtained on decompressing the hospital lock by dropping the pressure quickly to 10 or 15 lb. gauge pressure and then letting off the remaining pressure slowly. In any individual case, two or more recompressions might be necessary.

Bornstein (*2154*) 1910 gave the following decompression table in use at the construction work at Hamburg:

After the following times in compressed air:	Decompression rate:
Less than 50 minutes	1 atmosphere in 10 seconds.
1 to 2 hours	1 atmosphere in 5 minutes.
2 to 3 hours	1 atmosphere in 10 minutes.
4 to 5 hours	1 atmosphere in 20 minutes.
7 to 8 hours	1 atmosphere in 20 minutes.

Bornstein found little or no difference in the incidence of "bends" with the uniform decompression or Haldane's stage method. It should be noted, however, that Zuntz (*2217*)

1909 had recommended Haldane's method for the protection of compressed air workers.

There is no evidence, according to Hill (*2172a*) 1910 that a 3-hour working period is more dangerous than a 1½-hour period or that 8 hours is more dangerous than 3. Actually, Hill agreed with Keays that the danger is lessened when there is only 1 decompression. Hill used the following decompression schedule:

Decompression from 40 to 29 lb. in 5 minutes, hold for 10 minutes;
Decompression from 29 to 12.6 lb. in 8 minutes, hold for 10 minutes;
Decompression from 12.5 to 0 lb. in 15 minutes, hold for 10 minutes.

In testing uniform decompression, Hill decompressed from a pressure of 75 lb. to zero at a rate of 20 minutes per atmosphere or 14.7 lb. Greenwood, as subject, was decompressed from a level of 92 lb. pressure in 2 hours and 17 minutes. Hill recommended one stage at 15 lb. pressure for workers in caissons up to 50 lb.; 15 minutes at 10 lb. for workers in caissons up to 30 lb.; and 30 minutes at 15 lb. pressure for workers in caissons up to 45 lb. gauge. He pointed out that Hersent used a modified stage decompression method. The total time for decompression from various atmospheres according to Hersent is given in the following table:

After 1 hour at the following pressures (atmospheres)	Decompression time (minutes)
Plus 2½	26
Plus 3	46
Plus 3½	60
Plus 4	77
Plus 4½	100
Plus 5	150
Plus 5½	183

Hill's paper (*2173*) published in 1910–11 contains a comprehensive review of the general field of caisson disease. Hill found no pronounced superiority of the stage method of Haldane over the uniform method of decompression. Bornstein's comparison between the stage and the uniform method, carried out from 29-lb. pressure, did show a slight advantage for the stage method, but the differences, according to Hill, lay within the limits of experimental error. Bornstein reported better results by allowing the men to climb a ladder 25 m. high to increase the circulation and pulmonary ventilation.

Hill emphasized the alleged importance of muscular work in preventing symptoms of caisson disease and it was believed that breathing oxygen helped to hasten clearance of nitrogen. Hill pointed out that it is generally held that increasing the length of the shift increases the risk to workers. There was no conclusive evidence, however, in Keay's table (*2176*) based on 557,000 man-shifts at the East River tunnels, that shifts of 3 hours were more dangerous than 1½-hour shifts or 8-hour shifts more dangerous than 3-hour shifts. Since bubbles persist for a long time and act as starting points for other bubbles, Hill believed it wise to have long-time intervals between successive shifts. Bubbles had been seen in the veins of animals killed as long as 45 hours after decompression and they might last for many days within the tissue of the spinal cord. It seemed, therefore, that given periods of work in the caisson, if carried out too close together, might have cumulative effects.

Hill emphasized the value of recompression and subsequent slow decompression in the treatment of caisson disease. He stressed the importance of avoiding delay in recompressing the patient and pointed out that irreversible damage to nerve tissues may otherwise result. He concluded that the decompression times recommended by the Admiralty Committee were unnecessarily long and could be shortened with safety, especially if the men exercised during decompression. Hill believed that while the stage method was not as superior to the uniform decompression method as the Committee maintained, nevertheless, the stage method could be made reasonably safe and was most suitable for caisson operations. Hill considered that a first stage at 8 lb. pressure for 15 minutes was sufficient after a shift at a working pressure of 30 lb. and that a first

stage of 30 minutes at 15 lb. pressure was adequate after a shift at 40 to 45 lb. pressure. Five minutes in the first case and 10 minutes in the second should, Hill believed, be allowed for completing the decompression.

2. REGULATIONS FOR CAISSON AND TUNNEL WORKERS

In 1911, Langlois (*2179*) stated that no decompression code could be adopted in France because of a law forbidding the regulation of hours of labor. However, the usual hours of work were as follows:

8 hours under pressure below 2 kg. excess pressure,
7 hours under pressure between 2 to 2.5 kg. excess pressure,
6 hours under pressure between 2.5 to 3 kg. excess pressure,
5 hours under pressure between 3 to 3.5 kg. excess pressure,
4 hours under pressure between 3.5 to 4 kg. excess pressure.

These working times included the time of "locking in" and "locking out." Langlois stated that "locking out" should occupy at least 50 minutes for all pressure above 3 atmospheres (absolute). Langlois listed various decompression systems as follows:

(*a*) The Austrian system which was a uniform decompression at a rate of 0.1 atmospheres or 1.5 lb. in 2 minutes.

(*b*) The French system, requiring 20 minutes per kg. for pressures above plus 3 kg., 15 minutes per kg. for working pressures between plus 3 and plus 2 kg., and 10 minutes per kg. for working pressures between plus 2 kg. and normal pressure.

(*c*) The Dutch system which required 30 minutes per kg. for working pressures above plus 3 kg., 20 minutes per kg. for pressures between 1.5 and 3 kg., and 15 minutes per kg. for pressures between 1.5 kg. and normal pressure.

For a review of regulations governing hours of work and times of decompression in effect and under consideration up to 1912, the reader should consult the report by Japp (*2174*) who was managing engineer for S. Pearson and Son in charge of construction of the East River tunnels for the Pennsylvania Railroad. Keays was medical officer in this construction operation. At gauge pressures to 32 lb., the men worked 8 hours out of 24, taking a one-half hour interval for lunch either under the working pressure or a slightly reduced pressure. Above working pressures of 32 lb., the men worked in shifts of 3 hours with 3-hour rest intervals. The working pressure never exceeded 42 lb. gauge. Decompression was carried out with 3 locks. Japp included in his report the following table based on Haldane's theory:

Working pressure (gauge)	Reduce pressure in 3 minutes to	Total time in lock after 8 hours' work	Total time in lock after 3 hours' work	Total time in lock after 2 hours' work
Pounds	*Pounds*	*Minutes*	*Minutes*	*Minutes*
27	6	9	—	—
30	7½	24	—	—
32	8½	33	—	—
35	10	—	25	—
40	12½	—	35	—
42	13½	—	51	37
45	15	—	—	42
50	17½	—	—	48

At this time the Air Worker's Union stipulated a change to the following hours of work:

Hours of work	Working pressure (gauge) (pounds)
2 shifts of 3¾ hours each	Up to 22.
2 shifts of 3 hours each	Up to 33.
2 shifts of 2 hours each	Up to 35.
2 shifts of 1½ hours each	Up to 40.
2 shifts of ⅔ hours each	Up to 45.

The following comparison between uniform and stage decompression was given by Japp:

Tunnel pressure (gauge) (pounds)	Hours worked	Uniform decompression (minutes)	Stage decompression (minutes)
28	2 shifts of 3¾	18⅔	14
36	2 shifts of 3	24	36
41.99	2 shifts of 2	42	37
45.99	2 shifts of 1½	46	35
50	2 shifts of 1	50	33

A useful review of the rules then current for workers in caissons and compressed air generally was published by Silberstern (*2203*)

in 1912. He stated that for pressures over plus 1 atmosphere, only rugged persons should be permitted to work. Applicants with ear drum lesions, nasal catarrh, obesity, alcoholic tendencies, circulatory or respiratory diseases, nerve disease, kidney disease, bladder troubles, or gonorrhea should be excluded, and the upper age limit should be set at 40 years. Physical examinations were given to new workers before going into high pressures and to any worker after illness or after more than a 2-day absence from work. Physical examinations were given every 3 months. Compression was carried out with care so as to avoid trauma to the ears. The rate of "locking in" was never greater than 0.1 atmospheres or 1.5 lb. per ½ minute. For new workers, the rate was slower—no more than 0.1 atmospheres or 1.5 lb. in 1 minute. Working hours were recommended as follows:

Plus 1 to 2 atmospheres, 2 shifts of 4 hours each.
Plus 2 to 2.5 atmospheres, 2 shifts of 3 hours each.
Plus 2.5 to 3 atmospheres, 2 shifts of 2 hours each.
Plus 3 to 3.5 atmospheres, 2 shifts of 1 hour each.

If excess pressure was over 1½ atmospheres, neophytes were tested by being allowed to remain in the caisson for a preliminary period of 1 hour. The first work period was set at ⅓ of the regular work shift and the second at ⅔ of the regular shift. If the pressure was less than plus 1 atmosphere, there was no need to restrict the time of exposure. The first half of the "locking-out" period was to last three-quarters minute for every fall in pressure of 0.1 atmospheres or 1.5 lb. and during the second half, decompression was to be carried out at a rate of 3 minutes for each atmosphere or 14.7 lb. If the pressure was more than plus 1 atmosphere or 14.7 lb., the entire decompression was conducted at a rate of three-quarters minute for each 0.1 atmosphere or 1.5 lb.

In caisson or tunnel operations where the pressure was more than plus 1.5 atmospheres, it was required that medical supervision be provided and a recompression lock was mandatory. Other precautionary measures for the protection of workers included protection against cold, adequate ventilation, electric lighting, and training of workers in the means by which they can protect themselves from the danger of high pressure. Regarding ventilation, it was considered that at least 50 cu. m. of air per man per hour should be supplied.

In reporting on accidents in compressed air in the course of the construction of a viaduct at Rouen, France, Lecaplain (*1104, 1201*) 1914, referred to a regulation of 15 December 1908 setting forth precautions to be taken for the prevention of compressed air illness. Compression time was required to be at least 4 minutes per kg. in going to working pressures up to 2 kg. gauge pressure. An additional 5 minutes was required for each kg. above 2 kg. gauge pressure. The decompression rate was set at 20 minutes per kg. if the working pressure was above 3 kg. per sq. cm. gauge pressure. When the working pressure was between 2 and 3 kg. per sq. cm., the decompression time was 15 minutes per kg. For working pressures of 2 kg. to 0 gauge pressure, a decompression rate of 10 minutes per kg. was prescribed. If the working pressure was not above 1 kg. per sq. cm., then the total decompression time could be reduced to 5 minutes.

It was required that the working chamber be sufficiently large that workmen could stand erect and ventilation should be provided such that the carbon dioxide concentration should not rise above 0.01 percent. A recompression chamber large enough to receive a patient and 2 attendants was to be provided in any operation in which the pressure in the working chamber was over 2 kg. per sq. cm. An *Arrêté* of 28 December 1908 fixed the duration of work as follows:

In gauge pressures of less than 2 kg., not more than 8 hours in 24 hr.
In gauge pressures between 2 and 2.5 kg., not more than 7 hours in 24 hr.
In gauge pressures between 2.5 and 3 kg., not more than 6 hours in 24 hr.
In gauge pressures between 3 and 3.5 kg., not more than 5 hours in 24 hr.
In gauge pressures between 3.5 and 4 kg., not more than 4 hours in 24 hr.

A detailed review of methods for the prevention and treatment of caisson disease is to be found in Erdman's article (*1067*) on compressed air illness published in 1916. He reviewed various recommendations for length

of shifts in compressed air and pointed out that in deciding on practical tables limiting the hours of labor of compressed air workers, fairness to the contractors as well as safety to the workers must be considered. The methods of uniform and stage decompression were considered in detail and their relative merits discussed. It is concluded that none of the suggested methods of decompression entirely eliminated cases of the "bends," but that the incidence could be very radically reduced. Active treatment by recompression was also discussed. This article by Erdman is to be recommended for readers who wish access to a discussion of the work of Hill, Haldane, Erdman, Boycott, Damant, Japp, von Schrötter, Ryan, and Keays.

In 1918, Erdman (*2164*) referred to a standard legislative bill for the prevention of compressed air illness. It was prepared by the American Association for Labor Legislation and was adopted without change as a State law in New Jersey in 1914. It is almost identical in many of its provisions with the New York State bill passed in 1909. However, the New Jersey bill provided for shorter hours of labor. Erdman agreed with the provisions of the bill with the exception that he believed that no work should be allowed where air pressure exceeds 50 lb. He advocated adoption of the stage method of decompression for tunnel workers.

In 1921, Leymann (*2182*) published German regulations for the protection of compressed air workers.

For a definitive report on the medical problems associated with the building of the tunnels under the East River under the supervision of the Public Service Commission for the First District of the State of New York between 1914 and 1919, the reader should consult Levy's article (*2181*) published in 1922. Levy believed that data derived from the East River tunnel operation did not permit conclusions as to the relation of age of workmen and incidence of decompression sickness. He was opposed to the rule that no man with a tendency to obesity be employed. He believed that the temperature and humidity of the working areas had little if any influence upon the number of cases of compressed air illness. No cases of decompression sickness occurred among 188,496 decompressions carried out below 15 lb. gauge pressure. At working pressures from 15 to 22 lb. gauge, there were 16 cases out of 621,342 decompressions. At these pressures, the workmen worked 8 hours a day. All cases were trivial. It was, therefore, considered perfectly safe for healthy men to work at pressures up to 22 lb. gauge for 8-hour shifts. At working pressures from 22 to 30 lb. gauge, the shifts were divided into two 3-hour periods with rest intervals of 3 hours. Under these conditions, there was a gradual rise in the number of cases with an increase in working pressure, a sharp peak occurring at 29 lb. pressure. The incidence of decompression sickness fell sharply at a working pressure of 30 lb., this being due obviously to the fact that between 30 and 35 lb. gauge pressure, workmen worked for only two 2-hour shifts daily with a rest interval of 2 hours between shifts. The relative number of cases at 35 lb. was less than that at 34 lb., again probably due to the reduction of labor hours between 35 and 40 lb. (two 1½-hour periods with a 3-hour rest period).

Levy suggested that increased safety of workers would be attained by changing to the 2-hour shift at a working pressure of 29 lb. instead of 30 lb. and to the 1½-hour shift at 34 lb. working pressure instead of 35 lb.

The following table provides a comparison between the hours of labor in force in the Pennsylvania Railroad tunnel under the medical supervision of Keays and the Public Service Commission tunnels under the East River under Levy's medical supervision:

Public Service Commission Tunnels
(Levy)

Gauge pressure (pounds)	Total hours of work per day	Shifts, hours		
		On	Off	On
1 to 22	8	4	½	4
22 to 30	6	3	1	3
30 to 35	4	2	2	2
35 to 40	3	1½	3	1½
40 to 45	2	1	4	1
45 to 50	1½	¾	5	¾

Pennsylvania Railroad Tunnels
(Keays)

Gauge pressure (pounds)	Total hours of work per day	Shifts, hours		
		On	Off	On
1 to 31	8	4	½	4
	—	—	—	—
	—	—	—	—
	—	—	—	—
32 to 42	6	3	3	3
	—	—	—	—

Comparison of the percentage of cases of caisson disease based on the number of decompressions from working pressures of 40 lb. or more indicates a definite decrease in incidence of decompression sickness in the Public Service Commission tunnels:

	Number of Decompressions	Working pressure, (pounds)	Number of cases	Percent of cases
Pennsylvania tunnels	8,510	40	139	1.63
Public Service Commission tunnels	5,325	41	5	0.094
	8,456	42	12	0.142
	5,730	43	6	0.105
	4,702	44	1	0.021
	33,035	45	24	0.073

In the tunnels of the Public Service Commission, men were "locked out" by a stage method of decompression. However, the initial drop in pressure was to ½ *gauge* pressure and not absolute pressure. Levy's paper may be consulted for résumés of the regulations of the New York State Labor Department and the laws governing workers in compressed air in the States of New Jersey and Pennsylvania. The regulations of the New York State Labor Department effective 1 March 1920 provided for the following hours of labor:

Working pressure (gauge) (pound)	Hours of labor in 24 hours		
	First shift, hours	Rest interval, hours	Second shift, hours
0 to 21	4	½	4
22 to 29	3	1	3
30 to 34	2	2	2
35 to 39	1½	3	1½
40 to 44	1	4	1
45 to 49	¾	5	¾

The New York decompression schedule provided for a rapid drop to one-half the maximum gauge pressure at a rate of 5 lb. per minute. The remaining decompression was stipulated at a uniform rate and the total time was to be equal to the time specified for the original maximum pressure as follows:

(a) 0 to 14 lb., decompression at a minimum rate of 3 lb. per minute.
(b) 15 to 19 lb., decompression at a minimum rate of 3 lb. per minute.
(c) 20 to 29 lb., decompression at a minimum rate of 3 lb. every 2 minutes.
(d) 30 lb. or more, decompression at a minimum rate of 1 lb. per minute.

Other provisions of the regulations dealt with ventilation after blasting, wash room and rest room facilities, medical attendance, physical examinations, etc.

According to the New Jersey law (Acts of 1914, ch. 121), the hours of labor were the same as the New York regulations. The law provided that, except in emergency, no persons would be allowed in any caisson or tunnel when the pressure exceeded 50 lb. gauge. For tunnel workers, the decompression rate was set at 3 lb. per 2 minutes, except when the working pressure exceeded 36 lb. when it should be 1 lb. per minute. For caissons, the following decompression times were used:

Working pressure (pound)	Total decompression time (minutes)
0 to 10	1
11 to 15	2
16 to 20	5
21 to 25	10
26 to 30	12
31 to 36	15
37 to 40	20
41 to 50	25

According to an Act of 19 July 1917 of the State of Pennsylvania, the maximum hours of labor prescribed were the same as for the State of New Jersey. The rates of decompression were also the same as those set forth in the New Jersey Act.

State of New York's Industrial Code Bulletin No. 22-22a, effective 1 May 1922 set forth industrial code rules as amended, relating to work in compressed air tunnels and caissons, and to tunnel construction. Rule No. 1151 provided that the working time in any 24 hours should be divided into two shifts under compressed air with an interval in open air. Those who had not previously worked in compressed air should work but one shift during the first 24 hours and no person should be subjected to pressures exceeding 50 lb. per sq. in. except in an emergency. The maximum number of hours to each shift and minimum open air interval between the shifts during any 24 hours for any pressure were set forth as follows:

Working Pressure (gauge) (pounds)	Hours of labor in 24 hours			
	Maximum	First shift	Minimum rest interval	Second shift
0 to 18	8	4	½	4
18 to 26	6	3	1	3
26 to 33	4	2	2	2
33 to 38	3	1½	3	1½
38 to 43	2	1	4	1
43 to 48	1½	¾	5	¾
48 to 50	1	½	6	½

According to Rule No. 1152, no person employed in compressed air should be allowed to pass from the working area into normal air except after decompression carried out in an intermediate lock, according to a stage method in which a drop of one-half of the maximum gauge pressure should be at the rate of 5 lb. per minute. The remaining decompression should then be carried out at a uniform rate and the total time of decompression should be equal to the time specified for the original maximum pressure as follows:

Working pressure (gauge) pounds	Decompression time
0 to 15	3 pounds per minute.
15 to 20	2 pounds per minute.
20 to 30	3 pounds per 2 minutes.
30 or over	1 pound per minute.

Two papers published in 1928 may be consulted. The first is that of Draeger (*2162*) who recommended a decompression time of 90 minutes from a working pressure of plus 3 atmospheres or 45 lb. The second is that of Tanaka (*2208*) who described treatment of caisson disease by means of a recompression chamber.

The reader is also recommended to consult Wright and Brady's article on compressed air illness (*1162*) 1929. This paper covers the history of the development of our knowledge of decompression sickness and contains a description of tunneling operations. Reports of Keays and Erdman on the incidence of decompression sickness are given as well as mortality figures in various caisson and tunneling works. A clinical picture of the disease is reviewed and post-mortem findings and predisposing factors are considered. Various recommendations concerning hours of labor, ventilation, working temperature, decompression time, and recompression treatment are given. Wright and Brady's article is recommended to those desiring a comprehensive but brief review of the status of knowledge of caisson disease up to 1929.

In 1930, De Veaux (*2161*) medical examiner for the Central Maine Power Company in the Wyman Dam in the State of Maine published the following tables for hours of work and decompression time in force on the Wyman Dam construction:

Working pressure (gauge) pounds	Hours of work in 24 hours	Total time for decompression, minutes
0 to 22	8	12
22 to 26	6	18
26 to 32	4	22
32 to 36	3	26
36 to 41	2	28
41 to 50	1	32

In decompression, the pressure was dropped rapidly to one-half gauge pressure and then slowly to normal.

Singstad (*39*) 1936 discussed in some detail the safety codes for work in compressed air. By 1936, codes had been adopted by New York, New Jersey, Massachusetts, Pennsylvania, Wisconsin, Ohio, Maine, and California. The codes of California, Massachusetts, Maine, and New York were at that time in accord as to hours of labor and decompression schedules. In 1910, the following hours of labor were prescribed by the New York code:

Working pressure (gauge) pounds	Hours of labor in 24 hours		
	First Shift	Rest Interval	Second Shift
0 to 27.99	8 hours with 30-minute interval		
28 to 35.99	3	1	3
36 to 41.99	2	2	2
42 to 45.99	1½	3	1½
46 to 49.99	1	4	1

In 1910, the New York code prescribed uniform decompression at a rate of 3 lb. for every 2 minutes up to 36 lb. For over 36 lb. per sq. in., a rate of 1 lb. per minute was adopted. New York in 1922, Massachusetts in 1930, Maine in 1931, and California in 1933 adopted the following schedule of hours of labor:

Working pressure (gauge) pounds	Hours of labor in 24 hours		
	First shift	Interval	Second shift
0 to 18	4	½	4
18 to 26	3	1	3
26 to 33	2	2	2
33 to 38	1½	3	1½
38 to 43	1	4	1
43 to 48	¾	5	¾
48 to 50	½	6	½

Decompression was by the stage method according to a rate already given (*39*).

The Wisconsin schedule of hours of labor for tunnel workers was given (*39*) as follows:

Working pressure (gauge) pounds	Hours of labor in 24 hours		
	First shift	Rest Interval	Second shift
0 to 21	4	½	4
21 to 30	3	1	3
30 to 35	2	2	2
35 to 40	1½	3	1½
40 to 45	1	4	1
45 to 50	¾	5	¾

The Wisconsin code provided that tunnel workers be decompressed at a uniform rate of 3 lb. per 2 minutes when the working pressure was 36 lb. per sq. in. or less and at a rate of 1 lb. per minute when the gauge pressure was above 36 lb. The Wisconsin schedule for hours of work in caisson operations was the same as those for New York, Massachusetts, Maine, and California. For workers in caissons, the following schedule for decompression was prescribed by the Wisconsin code:

Working pressure (gauge) pounds	Minimum decompression time (minutes)
0 to 10	1
10 to 15	2
15 to 20	5
20 to 25	10
25 to 30	12
30 to 36	15
36 to 40	20
40 to 50	25

The Pennsylvania rules for caisson and tunnel works established the same working hours as the Wisconsin code for tunnels. The Pennsylvania decompression schedule was the same as that for New York. The New Jersey

rules, as published in 1931, prescribed the same hours of work and rest for caisson workers and tunnelers as New York. The decompression schedules for caissons and tunnels in New Jersey are the same as those for Wisconsin. It should also be noted that Wisconsin provided a stage compression with stops at every 5 lb. pressure to determine whether anyone in the lock was "blocked."

In 1926, the Province of Ontario, Canada, published a code governing most of the regulations common to the State codes in the United States. The hours of labor closely followed the Pennsylvania and Wisconsin codes and a stage decompression identical with the New York code was established. Decompression rules were required to be observed by all workers remaining under pressures of 15 to 27 lb. for over 30 minutes, or 27 to 31 lb. for over 15 minutes, and for all subjected to a pressure of 31 lb. or more. For pressures of 22 lb. or greater, workers were required to remain at the place of work for 1 hour after decompression.

Singstad (*39*) 1936 referred to the Committee on Regulations for Work Carried Out Under Compressed Air, appointed by the Council of the Institution of Civil Engineers in Great Britain on 30 April 1935. In a report submitted in January 1936, this committee recommended the following hours of labor:

Working pressure (gauge) pounds	Hours of labor
0 to 25	One period not exceeding 8 hours including one-half hour for meal.
25 to 40	One 6-hour period including one-half hour for meal.
40 to 50	One 4-hour period with a meal during a decompression.

After working at pressures between 25 and 40 lb., men were to remain at the working place at least 40 minutes after decompression. After working at pressures between 40 and 50 lb., men were to be detained for 1 hour before leaving the work. The committee favored a single working period schedule rather than the 2-period schedule generally used. They did not believe that remaining under pressure beyond the period for body saturation (4 to 5 hours) added materially to the danger.

Quadri (*2195*) 1937 recommended the following times for compression and decompression:

COMPRESSION

Working pressure (atmospheres)	Total time of compression (minutes)
Plus 0.5	3
Plus 1	5
Plus 1.5	8
Plus 2	12
Plus 2.5	16
Plus 3	22

DECOMPRESSION

Working pressure (atmospheres)	Total time of decompression (minutes)
Plus 0.5	5
Plus 1	8
Plus 1.5	16
Plus 2	24
Plus 2.5	36
Plus 3	55

In 1938 Pancheri (*2189*) gave maximum hours of labor in caissons in Italy.

In 1938 Stammberg (*2205*) published a report of his experience as medical officer at the construction of a bridge in Estonia by the firm of Höjgaard and Schultz A/S, Copenhagen, during the period between March and December 1937. During this time, 4 caissons were sunk. There were 3 shifts per day with an average of 15 men working per shift. The Estonian rules regarding hours of labor were given as follows:

Working pressure (atmospheres)	Hours of labor
0 to plus 1	7
Plus 1 to 2	6.5
Plus 2 to 2.5	6
Plus 2.5 to 3	5

These times included the periods of "locking in" and "locking out."

The following table of hours of labor and times of decompression was recommended by Cushing (*2159*) 1940, who was medical director of the S. A. Healy Company, which constructed the City of Detroit's sewage disposal plant and associated tunnels:

Working pressure (gauge) pounds	Hours of work	Total time of decompression (minutes)
5 to 18	8 (½ hour off)	5 to 10
18 to 25	6 (3 on and 3 off)	10 to 15
25 to 32	4 (2 on and 2 off)	15 to 20
32 to 38	3 (1½ on and 6 off)	20 to 25
38 to 43	2 (1 on and 6 off)	25 to 30
43 to 48	1½ (¾ on and 6 off)	35 to 40
48 to 50	1 (½ on and 6 off)	40

In 1943, Cruthers, Geenens, Conover, Levy, and Legget (*2158*) presented discussions of the Queens Midtown tunnel construction. The reader should consult Levy's discussion in this connection for a modern consideration of the protection of compressed air workers. Levy compared the working conditions in the Queens Midtown tunnel with those of the Pennsylvania Railroad tunnel. In the latter construction, no legal regulations were imposed for pressures up to 35 lb. The working day was 8 hours long with one-half hour rest period. For gauge pressures of 32 to 42 lb., the men worked for two 3-hour shifts with a 3-hour rest interval. A maximum decompression rate of 2 lb. per minute was prescribed. It appeared according to Levy (*2158*) that a practical limit of working hours has already been reached. He believed that it is possible to carry shortening of hours to a point where the cost of compressed air tunneling becomes prohibitive.

The New York State law provides that whenever the pressures exceed 26 lb. gauge, there must be 2 air chambers in use in the tunnel, the outer chamber not to exceed one-half the pressure in the heading. Using a single bulkhead with no outer chamber, 270,672 decompressions were carried out from a 22 to 37.5 lb. pressure range with 486 cases of decompression sickness (0.179 cases per 100 decompressions). Using an additional bulkhead and outer chamber, 316,595 decompressions were carried out from the same pressure range with 646 cases of decompression sickness (0.204 cases per 100 decompressions). From these data, little advantage can be seen for the use of outer chambers as far as compressed air illness is concerned. Levy advised further study of the regulations inasmuch as the use of outer chambers and additional bulkheads might be found to be an unwarranted expense. Levy believed that exception might well be taken to the use of stage decompression in caissons and tunnels.

3. RECOMPRESSION TREATMENT

In 1909 and 1912, Keays (*1089*, *2176*) reported on the effects of recompression treatment of 3,692 cases of compressed air illness in workers during the building of the East River tunnel. Out of 3,278 cases of pain without other complicating symptoms, 90 percent were relieved by recompression. Of 47 cases complaining of pain with prostration, 38 were relieved or cured, 6 died, and 3 refused treatment. Of 80 cases involving the central nervous system, 4 cases of hemiplegia were cured permanently after recompression. There were 36 cases of sensory disturbances; 34 of these were relieved by recompression while 2 refused treatment. Of 34 cases with motor disturbances alone, 23 were benefited and 11 showed no improvement. Ten cases with both sensory and motor disturbances were recompressed; 9 of these were permanently relieved while 1 was improved. Out of 197 cases of vertigo, 108 enjoyed complete relief by recompression and 82 were partially relieved. Seven patients refused to undergo the treatment. There were 60 cases with dyspnea or shock and all of these were cured by recompression. There were 17 cases of collapse, of which 8 recovered after recompression and 9 died. It was felt that administration of oxygen in these cases gave no appreciable benefit.

Ryan (*1137*) 1912 believed that prompt and skillful recompression was indicated in caisson disease. He considered that raising the pres-

sure to the previous working pressure was dangerous and unnecessary. Recompression to two-thirds of the working pressure was considered adequate. Subsequent decompression of recompressed patients in mild cases was carried out at a rate of 4 minutes per lb. but in severe cases the decompression rate was 10 to 12 minutes per lb.

In 1917, Levy (*2180*) published a short article on precautions adopted by the New York Public Service Commission for the protection of the health of workers in compressed air. As physician to the commission, Levy referred to his work in enhancing safety conditions in the East River tunnel construction work. Recompression chambers were used in cases of decompression sickness, recompression being carried out to the pressure to which the patient was exposed in the working chamber. Pressure was then slowly reduced to normal. Stage decompression for "locking out" workmen from the chamber was stated to be a great factor in reducing accidents.

Concerning treatment of decompression sickness by recompression, De Veaux (*2161*) 1930 believed that the patient should be given just enough pressure in the medical lock to relieve symptoms. It was considered wise to allow double or even triple the normal decompression time for "locking out." In some cases at the Wyman Dam, Maine, decompression following therapeutic recompression lasted 4 to 5 hours. During the last 10 lb. of decompression in severe cases, oxygen was used, the patient breathing for 1 minute and then resting for 3 minutes, etc.

Behnke (*2152*) 1942 considered recompression to be the best treatment for compressed air illness. The minimum recompression pressure recommended was 45 lb. regardless of original exposure pressure. This was maintained for 30 minutes. If relief was complete, the decompression was begun. If the symptoms continued, however, the patient was maintained at pressure for 90 minutes more. Behnke advised inhalation of a helium-oxygen mixture (70 percent helium, 30 percent oxygen) during recompression. After compression had been maintained for a sufficiently long time, the pressure was to be allowed to drop uniformly to 27 lb. per sq. in. in 10 minutes. Then it was to be held at this pressure for 30 minutes, dropped to 20 lb. for 30 minutes following a 30 minute stage at 13.5 lb. and then brought to normal over a 5-minute period.

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2204. Singstad, O. Engineering problems related to the health of workers in compressed air. *Pacif. Sci. Congr.*, 1939, *6:* 53–83. [P, M, R]

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2207. Taylor, A. S. and J. Byrne. Stöffel's operation for caisson disease. *Med. Rec., N. Y.*,1919, *95:* 344.

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2209. Thomson, T. K. Pneumatic caissons. *Sci. Amer. Suppl.*, 1908, *66:* 232–236; 244–247. [P, R]

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2212. Verschuyl, J. A. Over den invloed van den arbeidsduur op het voorkomen van caissonziekte. *Ned. Tijdschr. Geneesk.*, 1904, *44*(2): 2139–2144. [P]

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2214. Waller, G. *De hygiène der caisson-arbeiders· (Fundeeringen onder hoogen luchtdruk)*. Amsterdam, F. Van Rossen, 1904, 29 pp. [R]

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2219. Anon. The limit of human endurance of high air pressures. *Engng News*, 1895, *34:* 67. [P]

B. DECOMPRESSION OF DIVERS

For detailed information on decompression tables for diving, the reader may refer to reports listed below and the *Diving Manual* (*42*). Readers having access to the closed literature should also consult that source of information for work on diving procedures developed during World War II.

Particular attention is drawn to the paper by Hawkins and Shilling (*2226*) 1936 on surface decompression of divers and to a report by Gouze (*2224*) 1944 on the use of surface decompression as a routine procedure in diving. Surface decompression involves bringing the diver from the bottom directly to the surface with limited decompression in the water, followed at once by recompression in a chamber with subsequent full decompression. The method was first employed in the salvage of the S–51 in 1925 because the cold water and tides made decompression in the open sea impracticable. As Behnke and Willmon (*1440*) 1939 have stated, surface decompression was used extensively in the salvage operations required to raise the U.S.S. *Squalus*.

Surface decompression permits the elimination of excess gas from body tissues under conditions of warmth and rest, and under adequate observation. The danger of surface decompression lies in the possible formation of extensive gas embolism during the interval between the removal of the diver from the water and his subsequent recompression on the surface. As Gouze (*2224*) 1944 has pointed out, the question is, what is the safe time interval between the last stop in the water and recompression in the chamber. In experiments designed to answer this question, 130 dives were made using surface decompression. The depth of the dives ranged from 66 to 108 ft. and the time on the bottom was 26 minutes to 166 minutes. The intervals between ascent to the surface and recompression ranged from 3.5 minutes to 14 minutes (average, 6.3 minutes). It was necessary to transport the subjects to a compression chamber on a barge 175 to 200 yards away, and, therefore, the time tended to exceed the 3- to 4-minute interval prescribed as a maximum by the *Diving Manual* (*42*) 1943.

Results indicated that the interval between surfacing and recompression might safely be prolonged under certain conditions to 14 minutes without the occurrence of "bends." However, it was believed important to reduce this interval to a period not exceeding 3 to 4 minutes in accordance with the *Diving Manual* (*42*). In the experiments in question, no case

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of "bends" occurred and divers suffered no apparent ill effects. Oxygen administration was not considered essential, but Gouze stated that its use tended to eliminate after-fatigue.

2220. Boinet, [ ]. Traitement de la maladie des scaphandriers. *Marseille méd.* 1907, *44:* 357–370. [R]

2221. Cazamian, [ ]. Plongées en scaphandre. Hygiène du scaphandrier. Prophylaxie et traitement des accidents. *Arch. Med. Pharm. nav.*, 1927, *117:* 105–129. [R]

2222. Damant, G. C. C. and E. R. Lockwood-Thomas. A case of compressed-air illness cured by recompression. *Brit. med. J.*, 1909, *2:* 881–882. [Ch]

2223. Dorello, F. La decompressione "mista" nel palombaro. *Ann. Med. nav. colon.*, 1936, *42:* 203–209. [P]

2223a. Glibert, D. Contribution à la prophylaxie du "mal des caissons." *Bull. Acad. Méd. Belg.*, 1912, Sér. 4, *26:* 640–659. [P, R]

2224. Gouze, F. J. A method and study of surface decompression as a routine procedure. *Nav. med. Bull., Wash.*, 1944, *42:* 578–580. [P]

2225. Hawkins, J. A., C. W. Shilling, and R. A. Hansen. A suggested change in calculating decompression tables for diving. *Nav. med. Bull., Wash.*, 1935, *33:* 327–338. [P]

2226. Hawkins, J. A. and C. W. Shilling. Surface decompression of divers. *Nav. med. Bull., Wash.*, 1936, *34:* 311–317. [P]

2227. Johannsen, E. W. Farerne ved dykning. *Ugeskr. Laeg.*, 1931, *93:* 915–918.

2228.* Kagiyama, S. Studies on prevention of caisson disease . On diving depth, resting time and safe time allowable for stay on bottom. *J. Kumamoto med. Soc.*, 1934, *10:* 562–564. [R]

2229. Maciel, H. Effeitos das variações da pressão atmospherica sobre o organismo humane. Tubistas, escaphandristas, alpinistas e aviadores. *Brasil-med.*, 1937, *51:* 77–86.

2230. Muto, P.-I. Nota circa un palombaro colpito da embolia gassosa tardiva, salvato per mezzo di una camera a comprimere improvvisata, sulla r. nave "S. Giorgio". *Ann. Med. nav. colon.*, 1923, *2:* 155–158.

2231. Perry, W. H. A case of caisson disease, or divers' paralysis, treated with compressed air. *J. Amer. med. Ass.*, 1923, *80:* 1455. [Ch]

2232. Phillips, A. E. Recent research work in deep sea diving. *J. R. Army Med. Cps.*, 1932, *59:* 34–45. [R]

2233. Repetti, G. V. Del nuovo metodo di immersione dei palombari in uso nella nostra Marina Militare. *Ann. Med. nav. colon.*, 1911, *2:* 186–221.

2234. Shimada, T. (A recovered case of caisson disease by means of re-diving.) *Bull. nav. med. Ass. Japan*, 1928–29, *17*(4): (Japanese text pagination), 24–26. (In Japanese.) [Ch]

2235. Soper, H. E. Times of decompression using oxygen and air. *Not. Proc. roy. Instn.*, 1930, *26*(2): 192–196. [P]

2236.* Zburzhinskiy, K. [Sanitary conditions in work of divers.] *Vo.-sanit. Dyelo*, 1932, no. 10, pp. 26–37.

C. OXYGEN ADMINISTRATION

1. ADMINISTRATION OF OXYGEN IN THE PREVENTION AND TREATMENT OF DECOMPRESSION SICKNESS

As a logical sequel to the gas bubble theory of decompression sickness, Paul Bert (*16*) 1878 suggested oxygen inhalation to replace nitrogen in the body and so to treat compressed air illness. On the same theory, Heller, Mager, and von Schrötter (*28*) 1900 also recommended oxygen administration in the treatment of decompression sickness. The reader will also find oxygen administration suggested in two reports by Mourilyan (*2244, 2245*) 1905 and 1906. Mourilyan stated that inhalation of oxygen under pressure during a dive made decompression less dangerous and its use after the onset of the symptoms of decompression sickness promoted separation of the gas from the body and assisted the circulation. Paul Bert and many subsequent investigators were aware of the danger of oxygen poisoning in any procedure involving the inhalation of oxygen under pressure and it is clear that a pressure will be reached at which inhalation of oxygen ceases to be an advantage in the prevention of decompression sickness because of oxygen intoxication.

Ham and Hill (*2241*) 1905–6 stated that rats could be decompressed rapidly from 20 atmospheres of oxygen without loss of life although there were convulsions. A similar decompression from 20 atmospheres of air was found to be fatal. However, since oxygen pressures of 50 lb. per sq. in. and above involved the danger of oxygen poisoning and since the hazards of decompression sickness below 50 lb. per sq. in. were not considered great, the use of oxygen during exposure to high pressures as a method of preventing decompression sickness was not believed to be particularly worthwhile.

Prevention of decompression sickness in deep-sea divers by oxygen inhalation is also

referred to in a brief report published in 1907 by von Schroetter (*2246*).

Twort and Hill (*2247*) 1911-12 carried out experiments in which human subjects breathed oxygen at a pressure of 3 atmospheres for 9 minutes and during subsequent decompression to normal atmospheric conditions. These investigators found that the nitrogen taken up by the urine under the conditions of compression is rapidly cleared by breathing oxygen under high pressure and regarded this an indication of the accelerated nitrogen clearance in the body as a whole. Fine, Frehling, and Starr (*2240*) 1934–35 observed that breathing 95 percent oxygen accelerated absorption of air from the peritoneal cavity and the soft tissues of rabbits. Denitrogenation of divers by breathing oxygen was discussed in 1934 by Dorello (*2239*).

Important modern contributions to our knowledge of oxygen administration as a therapeutic measure in decompression sickness have been made by Behnke and his associates. In 1935–36, Behnke, Shaw, Messer, Thomson, and Motley (*2237*) conducted experiments on dogs anesthetized with dial and urethane in which the animals were subjected to an air pressure of 65 lb. per sq. in. for 105 minutes and decompressed within 5 to 6 seconds. On decompression, the blood pressure first rose sharply and then fell steadily. The respiratory rate increased from an average of 21 to 81. The pulse rate fell from an average of 134 down to 94. The oxygen saturation of the arterial blood fell to 24 percent in one case and was below 70 percent in all cases. Animals were recompressed to a gauge pressure of 30 lb., oxygen being breathed by some animals and air by others. They were kept at 30 lb. pressure for 84 minutes followed by stage decompression lasting 30 minutes. Dogs breathing oxygen under these conditions showed a return to normal arterial oxygen saturation and a normal respiratory rate. At autopsy, only a few gas bubbles were found and these were seen in the peripheral veins. In the case of the dogs breathing air, the respiratory rate was increased; there was oxygen unsaturation and many bubbles were found, even in the arteries and in the heart, on sacrifice after return to normal pressure.

These experiments were again reported by Behnke and Shaw (*2238*) in 1937. Behnke and Shaw added that breathing oxygen during recompression did not relieve paralysis if this had already developed. However, on the basis of theoretical considerations and experimental evidence, it was stated that oxygen inhalation and recompression constituted an essential treatment for compressed air illness. Since pure oxygen can be breathed without discomfort by healthy individuals for 3 hours at 30 lb. gauge pressure, it was considered that 50 percent oxygen at 75 lb. gauge pressure could be tolerated for a corresponding time. Breathing 100 percent oxygen at 4 atmospheres (absolute) for more than 45 minutes may cause convulsions, fainting, and other symptoms of oxygen poisoning. In treating severe cases of compressed air illness (with prostration, asphyxia, and paralysis) it was recommended that recompression be carried out as follows: (*a*) The patient should be recompressed to a gauge pressure of 75 lb. breathing a 50 percent oxygen mixture, and maintained at this level for 15 minutes to 2 hours. (*b*) The pressure should then be lowered at a rate of 1 lb. per minute from 75 lb. down to 30 lb. pressure. At 30 lb. pressure, pure oxygen should be substituted and breathed for 1 to 2 hours. Pressure should then be reduced to normal at the rate of 1 lb. per minute and oxygen administration continued. If after 1 hour, the patient still has symptoms he should be recompressed to 30 lb. pressure and kept at this level for 24 hours, breathing air. He then breathes oxygen for 2 hours followed by decompression to normal. In mild cases, it was recommended that patients be recompressed to 30 lb. pressure and that they inhale pure oxygen at this pressure for 1 hour and then be returned to normal atmospheric pressure in 30 minutes. Symptomatic treatment was also outlined.

Further suggestions for the treatment of decompression sickness utilizing oxygen were made in 1939 by Yarbrough and Behnke (*2248*).

Jones, Crosson, Griffith, Sayers, Schrenk, and Levy (*2243*) 1940 reported that oxygen was administered for the last 20 minutes of decompression on the Queens Midtown tunnel construction in which the pressure in the tunnel was 34 to 37½ lb. per sq. in. and the rate of decompression during "locking out," 30 to 48 minutes. Out of 9,462 controls in which subjects breathed air during decompression, there were 12 cases of caisson disease while 23 cases of illness were reported in 11,196 subjects who breathed oxygen during decompression. There were, therefore, more cases of caisson disease reported by the oxygen group but it is probable that in the control group some mild attacks may not have been reported. All cases in the oxygen group were less severe than those of the controls. In spite of this, the experiments do not speak very strongly for the value of oxygen for decompression in tunneling and caisson work as a routine method of preventing decompression sickness. Oxygen administration in the treatment of caisson disease already developed is, of course, a different matter.

One of the most important single advances in the management of decompression sickness encountered in rapid reduction of pressure to levels below 1 atmosphere has been the development of our knowledge of pre-oxygenation in preventing aviators "bends," "chokes," and other symptoms of decompression sickness. The literature on this subject is not considered here in any further detail. Readers desiring such information are recommended to consult the literature cited by Hoff and Fulton (*3*) 1942 and Hoff, Hoff, and Fulton (*4*) 1944.

Recent investigations show that the gas pains associated with rapid decompression may also be relieved by pre-administration of oxygen. A report covering one such investigation is that of Henry, Lawrence, Bridge, and Williams (*2242*) 1944.

2237. Behnke, A. R., L. A. Shaw, A. C. Messer, R. M. Thomson, and E. P. Motley. The circulatory and respiratory disturbances of acute compressed-air illness and the administration of oxygen as a therapeutic measure. *Amer. J. Physiol.*, 1935–36, *114:* 526–533. [P]

2238. Behnke, A. R. and L. A. Shaw. The use of oxygen in the treatment of compressed-air illness. *Nav. med. Bull., Wash.*, 1937, *35:* 61–73. [P, R]

2239. Dorello, F. La deazotazione nel palombaro. *Ann. Med. nav. colon.*, 1934, *40:* 650–662. [P]

2240. Fine, J., S. Frehling, and A. Starr. Experimental observations on the effect of 95 per cent oxygen on the absorption of air from the body tissues. *J. thorac. Surg.*, 1934–35, *4:* 635–642. [P]

2241. Ham, C. and L. Hill. Oxygen inhalation as a means to prevent caisson and divers' sickness. *J. Physiol.*, 1905–06, *33:* vii-viiiP. [P]

2242. Henry, F. M., J. H. Lawrence, E. V. Bridge, and O. L. Williams. Protective effects of preoxygenation on abdominal gas pain. Results of a study of preflight breathing of oxygen on pain resulting from decompression to 38,000 feet. *War. Med., Chicago*, 1944, *6:* 395–397. [P, M]

2243. Jones, R. R., J. W. Crosson, F. E. Griffith, R. R. Sayers, H. H. Schrenk, and E. Levy. Administration of pure oxygen to compressed air workers during decompression: Prevention of the occurrence of severe compressed air illness. *J. industr. Hyg.*, 1940, *22:* 427–444. [P, R]

2244. Mourilyan, E. P. Compressed air illness and its treatment by the inhalation of oxygen. Pp. 179–183 in: *Statistical report of the health of the navy for the year 1904.* Eyre and Spottiswoode, London, 1905, ix, 197 pp. [R]

2245, Mourilyan, E. P. Compressed air illness and its treatment by the inhalation of oxygen. *J. trop. Med. (Hyg.)*, 1906, *9:* 286. [R]

2246. Schroetter, H. R. von. Die Berufskrankheit der Caissonarbeiter. Ueber ein prophylaktisches Verfahren—Verwendung von Sauerstoff von niederem Partiärdruck—zur Dekompression für Tieftaucher. *Int. Congr. Hyg. (Demogr.)*, 1907, *14*(2): 939–940. [P]

2247. Twort, J. F. and L. Hill. Further experiments on the effect of breathing oxygen on the nitrogen dissolved in the urine. *J. Physiol.*, 1911–12, *43:* xlii-xlivP. [P]

2248. Yarbrough, O. D. and A. R. Behnke. The treatment of compressed air illness utilizing oxygen. *J. industr. Hyg.*, 1939, *21:* 213–218. [P, R]

2. PHYSIOLOGICAL EFFECTS OF OXYGEN ADMINISTRATION

For the convenience of readers, particularly investigators interested in problems of oxygen poisoning and the use of oxygen in diving and caisson work, a number of references are given to literature on the physiological action of oxygen on the organism. These will be briefly discussed. Regarding the effect of oxygen on respiration, Kerr (*2272*) 1893 reported a decrease in the respiratory rate but no other

detectable effects. Schlesinger and Pembrey (*2278*) 1908 found that the rate of respiration decreased while the volume increased during oxygen administration. Further studies on the effect of oxygen on breathing have been reported by Barca (*2252*) 1914 and Bean (*2253*) 1929. Heck and Loeschcke (*2266*) 1942 stated that the carbon dioxide content of arterial blood fell when oxygen was breathed.

According to Hervé (*2268*) 1898, inhalation of oxygen by patients with anemia results in an increase in the number of red blood cells as well as an increase in the hemoglobin content of the blood. Case histories were given.

As will be seen by consulting the section on the therapeutic action of raised atmospheric pressures (p. 302), it has been held that an increase in the oxygen tension has therapeutic use in anemia. However, Anthony (*2249*) 1939 showed that the erythrocyte count as well as the hemoglobin content decreased when oxygen was breathed. The average diameter of the erythrocytes tended to fall, the heart rate slowed by about 10 percent, and the minute volume decreased by about 10 to 15 percent. If inhalation of oxygen was continued, the values tended to return toward normal again.

The effect of oxygen inhalation upon the frequency of the pulse was reported by Ekgren (*2261*) 1905, and Hill and Flack (*2270*) 1910 pointed out that oxygen administration permitted performance of a greater amount of muscular work and lessened the discomfort of forced breathing. According to Tinel (*2280*) 1927, respiration of oxygen results in a rapid progressive vasoconstriction of the cerebral arteries causing a diminution of the cerebral pulse. After breathing oxygen for a few minutes, the cerebral circulation was stated to return to normal.

Kümmel (*2275*) 1938, Barach and Steiner (*2251*) 1940, and Edson (*2260*) 1942 have reported on the effects of oxygen administration on the electrocardiogram. In the latter case, the subjects studied were cyanotic patients with cardiac insufficiency. Alterations were confined to changes in the RST-segment and the form of the T-wave. The changes were not uniform. Oxygen administration produced electrocardiographic changes in only 3 out of 20 noncyanotic control subjects.

According to Meyer (*2277*) 1923, brief exposures of canaries to 1 atmosphere of pure oxygen for 15 to 30 minutes at a time produced no effect upon metabolism. Bielschowsky and Thaddea (*2256*) 1923 found, on breathing pure oxygen, a fall in the carbon dioxide tension in the alveoli and a change in the acid-base equilibrium in the blood. Hypodermic administration of oxygen was stated by Gualco (*2262*) 1937 to cause a fall in basal metabolic rate and to have an excitant effect on hematopoiesis in patients and normal subjects.

According to Hahn and Niemer (*2263*) 1938, oxygen inhibits lactic acid formation in minced muscle. If the muscle preparation is allowed to stand for a while, oxygen no longer exerts this inhibitory action, but the effect can be reproduced by a muscle extract which does not in itself increase the muscle's utilization of oxygen. Further studies of this inhibition of lactic acid formation by oxygen were reported in 1939 by Hahn, Niemer, and Gasseling (*2264*) and by Heiting (*2267*) 1938. A further study by Hahn, Niemer, and Meisner (*2265*) 1940 may be consulted.

Breathing high oxygen mixtures has been shown by Kottke, Phalen, and Visscher (*2273*) 1944 to delay the onset of shivering in subjects exposed to a temperature of 10° C. and a humidity of 45 percent. Switching from air to oxygen during shivering results in a sensation of warmth while if the subjects are switched from oxygen to air during shivering, there is an increase in the intensity of the shivering. According to these investigators, however, oxygen has no effect upon the increased metabolic rate caused by shivering.

The action of oxygen on salivary secretion has been reported by Eddy (*2259*) 1931. The effect of administration of high oxygen percentages on sphincter and radial iris muscle reaction was reported by Bean and Bohr (*2254*) 1940.

According to Davidson (*2258*) 1925–26 breathing pure oxygen decreases the reaction time slightly. Much more profound effects are produced by respiration of low oxygen

than by respiration of high percentages of oxygen. Lehmann and Graf (*2276*) 1942 have reported that breathing pure oxygen at ground level improves the performance of human subjects in arithmetic tests, decoding, and recognition of letters.

For further studies on the physiological effects of oxygen, the reader should consult certain articles listed in the section on oxygen intoxication (p. 163), particularly, the review by Bean (*1445*) 1945.

2249. Anthony, A. J. Sauerstoffatmung, Blut und Kreislauf. *Luftfahrtmed.*, 1939, *4:* 11–13. [P]

2250.* Anthony, A. J. Die Zusammensetzung des Blutes bei Hyperoxämie. *Folia haemat., Lpz.*, 1940, *63:* 363–367. [P]

2251. Barach, A. L. and A. Steiner. Effect of inhalation of high oxygen concentrations with and without carbon dioxide, on the electrocardiogram. *Proc. Soc. exp. Biol., N. Y.*, 1940, *45:* 175–179. [P]

2252. Barca, L. Influenza delle inalazioni di ossigeno sulla meccanica respiratoria. Gazz. int. med.-chir., 1914, *17:* 529–537. [P]

2253. Bean, J. W. Effects of high oxygen pressures on blood acidity, oxygen consumption, volume flow of blood and respiration. *Proc. Soc. exp. Biol., N. Y.*, 1929, *26:* 832. [P]

2254. Bean, J. W. and D. F. Bohr. Sphincter and radial iris muscle reaction to high oxygen. *Amer. J. Physiol.*, 1940, *129:* 310. [P]

2255. Bergeret, P., P. Giordan, and M. V. Strumza. Travail musculaire en altitude et inhalation d'oxygène. *Travail hum.*, 1937, *5:* 129–149.

2256. Bielschowsky, P. and S. Thaddea. Über die Stoffwechselwirkung reiner Sauerstoffatmung. *Z. klin. Med.*, 1932, *120:* 330–340. [P]

2257.* Claussen, J. *Über den Einfluss von Kohlensäure- und Sauerstoffatmung auf den Muskeltonus beim Menschen.* Diss., Hamburg, 1940. [P]

2258. Davidson, B. M. Studies of intoxication. VIII. The influence of oxygen. *J. Pharmacol.*, 1925–26, *26:* 111–121. [P]

2259. Eddy, N. B. Regulation of respiration. The effect upon salivary secretion of an increased oxygen content of the inspired air and of forced ventilation. *J. Pharmacol.*, 1931, *41:* 423–433. [P]

2260. Edson, J. N. The effect of oxygen on the electrocardiograms of cyanotic patients. *Amer. Heart J.*, 1942, *24:* 763–773. [P]

2261. Ekgren, E. Zum Einfluss der Sauerstoffbäder auf Pulsfrequenz und Gefässtonus. *Z. klin. Med.*, 1905, *57:* 401–412. [P]

2262. Gualco, S. L'ossigenoterapia e la sua influenza sul metabolismo basale e sulla eritropoiesi. *Policlinico*, Sez. med., 1937, *44:* 577–592. [P]

2263. Hahn, A. and H. Niemer. Über die Hemmung der Milchsäurebildung durch Sauerstoff. *Z. Biol.*, 1938, *98:* 527–532. [P]

2264. Hahn, A., H. Niemer, and W. Gasseling. Über die Hemmung der Milchsäurebildung durch Sauerstoff. (4. Mitteilung.), *Z. Biol.*, 1939, *99:* 614–617. [P]

2265.* Hahn, A., H. Niemer, and E. Meisner. Über die Hemmung der Milchsäurebildung durch Sauerstoff. *Z. Biol.*, 1940, *100:* 358–360. [P]

2266. Heck, E. and H. H. Loeschcke. Wirkung hoher Sauerstoffteildrueke auf die Atmung. II Mitteilung. Die Lage der die Atmung regulierenden Zellgebiete im arteriovenösen Kohlensäuredruckgefälle. *Luftfahrtmed.*, 1942, *6:* 114–118. [P]

2267. Heiting, Hans. *Ueber die Hemmung der Milchsäurebildung in der Zelle durch Sauerstoff.* Diss. München, Heinr. und J. Lechte, 1938, 13 pp. [P]

2268. Hervé, F. De quelques effets physiologiques des inhalations d'oxygène, considérées au point de vue de leur action sur les globules sanguins dans la chlorose. *J. Méd. Bordeaux*, 1898, *28:* 30–33; 40–43. [P]

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3. OXYGEN ADMINISTRATION IN CLINICAL THERAPY

The references included under this heading, while not directly concerned with submarine or compressed air medicine, are nevertheless included because it is felt that they may be of use, particularly to investigators interested in further details on the effects of oxygen on the human body. For a historical approach to the subject of oxygen in clinical medicine, readers may consult papers by Kraus (*2352*) 1903, Galli (*2330*) 1908, Hahn (*2338*) 1899, Mamlock (*2360*) 1903–4, and Bainbridge (*2287*) 1908. In this latter paper, the reader will find reference to early suggestions of the clinical use of oxygen by Priestley, and Beddoes' use of oxygen and other gases in treating patients in the late eighteenth and early nineteenth centuries in England. These early attempts at oxygen therapy proved disappointing and this form of treatment fell into disuse.

For general studies on the therapeutic use of oxygen, the reader should consult papers by Michaelis (*2362*) 1900–1901; Aron (*7284*) 1901; Koch (*2348*) 1904; Barach (*2289*) 1923; Boothby, Mayo, and Lovelace (*2302*, *2302a*) 1939 and 1940; Hinshaw and Boothby (*2342*) 1942; and Andrews (*2281*) 1943. As Barach has stated, much of the skepticism concerning the value of oxygen therapy has been due to ineffective methods of oxygen administration. When used correctly for the proper indications, it is a valuable therapeutic technique. The reader should consult Andrews' monograph for techniques of oxygen therapy.

For reports on the use of oxygen in diseases of the lungs and other conditions in which anoxemia exists, the reader should consult reports by Van Baun (*2393*) 1889, Blodgett (*2299*) 1890, Catlin (*2307*) 1891, Blair (*2298*) 1892, Davis (*2317*) 1892, DeHaet (*2318*) 1895, Simpson (*2380*) 1896, Lodge (*2356*) 1900, Patton (*2367*) 1901–2, Vicars (*2394*) 1902, Bernabei (*2296*) 1903, Greene (*2333*) 1903, Haldane (*2339*) 1919, Barach (*2289*) 1923, and Davies and Gilchrist (*2316*) 1925.

For a consideration of treatment of diseases of the nose and ear with oxygen gas, the reader may consult a paper published by Stoker (*2384*) 1896. The use of oxygen in resuscitation is covered in reports by the following authors: Wauer (*2397*) 1920, Behnke (*2293*) 1941, Birnbaum and Thompson (*2297*) 1942, Gubar (*2335*) 1942, and Leigh and Richardson (*2354*) 1942.

Oxygen administration plays a definite role in the treatment of carbon monoxide poisoning. End and Long (*2322*) 1942 demonstrated that guinea pigs and dogs poisoned with carbon monoxide were quickly restored to consciousness by inhaling oxygen under 3 atmospheres of pressure. This was taken to indicate that the anoxia in these animals had been corrected. Such treatment also accelerated the elimination of carbon monoxide so that 30 minutes' treatment proved sufficient to remove most of the carbon monoxide from the animals' bodies. On the basis of these animal experiments, the authors proposed inhalation of oxygen under pressure in the treatment of human beings severely poisoned by carbon monoxide.

Honigmann (*2343*) 1891 believed that inhalation of oxygen was beneficial in cases of pernicious anemia and chlorosis, and Dreyer (*2320*) 1910 recommended breathing of oxygen in cases of extreme blood loss. In both these conditions, oxygen acts symptomatically and there is no question of a specific therapeutic effect of oxygen on the underlying anemic condition.

Baird (*2288*) 1895 discussed the action of oxygen in supporting cardiac function and Boland (*2300*) 1940 considered the use of oxygen in high concentrations for the relief of pain in coronary thrombosis and severe angina pectoris.

The use of oxygen in abdominal distention due to gas is discussed by the following authors: Grewal (*2334*) 1925, Rosenfeld and Fine (*2373*) 1938, Congdon and Burgess

(*2311*) 1939, and Fine and Starr (*2324*) 1939.

Schwab, Fine, and Mixter (*2379*) 1936 discussed the inhalation of 95 percent oxygen for 3 hours after encephalography to reduce the symptoms which normally follow this procedure.

A number of papers have been published on the action of gaseous oxygen applied locally or given by inhalation in the treatment of wounds and infections. Representative papers are those by Stoker (*2383*, *2384*, *2385*) 1896 and 1897, du Toit (*2391*) 1900, and Thiriar (*2388*) 1901. The administration of oxygen together with other substances such as alcohol vapor or carbon dioxide has attracted attention from time to time. In particular, the use of carbon dioxide with oxygen has been the subject of speculation and investigation in relation to raising tolerance to anoxia encountered at high altitudes. This literature will not be discussed but references to papers by the following authors are included: Crescenzi (*2313*) 1910, Willcox and Collingwood (*2398*) 1910, and Petrov (*2368*) 1943.

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4. OXYGEN APPARATUS AND OXYGEN GENERATORS

Reports on the preparation and purification of oxygen for therapeuric purposes by the following authors may be consulted: Mary (*2427*) 1891, Briggs (*2412*) 1924, Buttino and Navarra (*2416*) 1924, Schmidt and Krantz (*2436*) 1933, and two unsigned articles published in 1902 (*2439*) and in 1906 (*2440*).

A voluminous literature on oxygen inhalation apparatus has developed, particularly during World War II, and much of this is to be found as classified unpublished reports. A number of published reports on oxygen inhalation apparatus are included below to supply the reader with a background on this subject. The following authors may be consulted: Aulde (*2400*, *2401*) 1890; Brat (*2411*) 1905; Herff (*2424*) 1905; Rosenthal (*2433*) 1905; Wollenberg (*2438*) 1906; Moore (*2431*) 1909; Bayeux (*2406*) 1911; Hill (*2425*) 1912; Brunton (*2413*) 1913; Haldane (*2423*) 1917; Meltzer (*2428*) 1917; Barach (*2402*) 1922; Bourne (*2409*) 1922; Ryle (*2435*) 1922; Lian and Navarre (2426) 1923; Davies and Gilchrist (*2418*) 1925; Fine, Banks, and Hermanson (*2419*) 1936; Burgess (2415) 1937; Bulbulian (*2414*) 1938; Binet and Bochet (*2407*) 1940; and Barach and Eckman (*2404*) 1941.

The construction, management, and clinical use of oxygen chambers is discussed in reports by the following authors: Barcroft (*2405*) 1920, Binger (*2408*) 1925, Barach (*2403*) 1925–26, and Trusler and Meiks (*2437*) 1934.

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5. EXTRAPULMONARY ROUTES OF OXYGEN ADMINISTRATION

Many modes of oxygen administration other than by inhalation have been proposed at various times. These extrapulmonary routes are not of practical concern to medical officers entrusted with the care of submarine or diving personnel or caisson and tunnel workers. However, intravenous administration of oxygen is of theoretical interest in relation to gas embolism. For this reason, reports by the following authors have been included: Mariani (*2468*, *2469*, *2470*) 1901-2 and 1902, Gaertner (*2458*) 1902, Sciallero (*2475*) 1905, Neudörfer (*2472*) 1905, Rélier (*2473*) 1914, Tunnicliffe and Stebbing (*2480*) 1916, Galatà (*2459*) 1923, Singh (*2476*) 1935, Ishikawa (*2465*) 1939, and Ziegler (*2482*) 1941. Rélier stated that a 70 kg. man would tolerate intravenous injection of 840 cc. of oxygen and that the rate of intravenous injection of this gas should be slower in smaller animals than in large.

Tunnicliffe and Stebbing (*2480*) 1916 administered 500 to 1,000 cc. of oxygen intravenously to patients at rates of 600 to 1,200 cc. per hour. The oxygen was usually injected for 10 to 15 minutes at a time with 2- to 3- minute intervals in between. According to Singh, 5 cc. of oxygen could be administered intravenously in 10 minutes without danger to dogs, cats, and rabbits. If 10 cc. of oxygen were injected in 10 minutes, there was a rise in blood pressure and some evidence of embolism. Injection of 15 cc. of oxygen in 10 minutes resulted in death from embolism. Ishikawa found that dogs could safely absorb intravenously administered oxygen at a rate of

0.3 cc. per kg. body weight per minute for 10 to 15 minutes.

Ziegler's paper (*2482*) should be consulted for a review of the technique of intravenous injection of oxygen. The author believed that an intravenous injection rate of 200 to 1,000 cc. per hour for a 70 kg. man was ideal. Ziegler gave oxygen continuously at this rate for 9 hours. Claims were made for the value of intravenous oxygen therapy in the relief of cyanosis. It was stated to be contraindicated in patients with diminished lung capacity and marked dilatation of the right ventricle.

Subcutaneous injection of oxygen is another subject of little or no clinical concern to medical officers in the field of submarine and compressed air medicine. However, because of the theoretical applications of such literature to absorption of gases in tissues and the relation of decompression sickness, reports by the following authors are included: Ewart (*2455*) 1900, Thiriar (*2477*) 1901, Derose (*2451*) 1912, Bovier-Lapierre (*2447*) 1913, Howitt (2463) 1914, McCrae (*2471*) 1914, Grimberg (*2462*) 1916, Estabial (*2453*) 1920, Bayeux (*2445*) 1923, Lian and Navarre (*2467*) 1923, Campbell (*2450*) 1924–25, Agasse-Lafont and Douris (*2441*) 1925, Barker (*2444*) 1937, Evans and Durshordwe (*2454*) 1937, and Varskavskiy (*2481*) 1939. Intraperitoneal injection of oxygen is of similar theoretical interest and reports by Godwin (2461) 1912 and Bainbridge (*2442*, *2443*) 1913 and 1939 should be consulted.

Administration of oxygen by rectal injection of the gas has been discussed in papers by Kellogg (*2466*) 1887, Salomon (*2474*) 1903–4, and Burwash (*2448*) 1905.

For a discussion of the therapeutic use of oxygen-liberating solutions, the reader may consult papers by Gellé (*2460*) 1896, Thiriar (*2478*) 1904, Foderá (*2456*) 1905, Isaksohn (*2464*) 1905, and Bernabei (*2446*) 1909–10.

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2455. Ewart, W. The subcutaneous administration of oxygen. A note on the hypodermic injection of oxygen gas and of solutions of peroxide of hydrogen. *Brit. med. J.*, 1900, *2:* 1099–1101.

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2474. Salomon, H. Über Versuche extrabukkaler Sauerstoffzufuhr. *Z. diätet. phys. Ther.*, 1903–04, *7:* 559–566.

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2476. Singh, I. Intravenous injection of oxygen with the animal under ordinary and increased atmospheric pressure. *J. Physiol.*, 1935, *84:* 315–322.

2477. Thiriar, J. Die Behandlung des Furunkels und Anthrax mit Sauerstoff. *Allg. wien. med. Ztg.*, 1901, *46:* 118–119.

2478. Thiriar, [ ]. La méthode oxygénée. *J. Méd. Paris*, 1904, Sér. 2, *16:* 376–377.

2479. Thiriar, [ ]. La méthode oxygénée. *Rép. Thér.*, 1904, *21:* 519–521.

2480. Tunnicliffe, F. W. and G. F. Stebbing. The intravenous injection of oxygen gas as a therapeutic measure. *Lancet*, 1916, *2:* 321–323.

2481.* Varskavskiy, K. [On the question of the therapeutic effect of subcutaneous and intravenous administration of oxygen.] *Vo.-sanit. Dyelo.*, 1939, No. 10: 19–21.

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2483. Anon. L'injection intraveineuse d'oxygène chez l'homme. *Sem. méd., Paris*, 1902, *22:* 243–244.

D. HELIUM ADMINISTRATION

1. DISCOVERY AND PROPERTIES OF HELIUM

Two reports should be consulted by those wishing to gain access to information about helium with particular reference to its uses in compressed air work, diving, and the treatment of disease. The first of these is a paper by Stewart (*2487*) published in 1933 and the second is Shilling's report (*2486*) which appeared in 1941. Both papers have excellent bibliographical lists. A brief summary of their contents follows: In 1866, Lockyer (see *2487*) conceived the idea of examining sunspots and solar prominences with the spectroscope. In the course of these observations, he noticed a line in the yellow part of the spectrum which was more refrangible than the two already known D-lines referable to sodium. This new line he fixed on November 15, 1868 at a point designated D3. Lockyer and Frankland both thought that this line might be due to hydrogen visible under special solar conditions. However, after trying unsuccessfully by exhaustive experiments to reproduce the line with hydrogen, Lockyer became convinced that it was due to some element in the sun then unknown on the earth. He gave it the name "helium" (from the Greek word, *ἥλιος*, meaning sun.)

In 1895, Ramsay secured a sample of cleveite, one of the uranium-bearing minerals, powdered it and boiled it with weak sulfuric acid and extracted from it a sample of gas showing the spectrographic lines of argon and also the brilliant yellow line of helium. By this discovery, helium was thus recognized as a constituent of the earth's surface. Kayser of Bonn discovered helium as a component of the earth's atmosphere by spectroscopic methods, and in the summer of 1900, Ramsay and Travers separated helium from the other gases of the atmosphere.

At first, various radioactive minerals such as cleveite, pitchblende, etc., were the only source of helium. The gas could be obtained in only small quantities and cost as much as $2500.00 per cu. ft. In 1903, gas from a gas well in Dexter, Kans. was found to contain 1.84 percent helium. At the present time, this valuable gas is obtained commercially by ex-

traction from natural gases. So far, it appears that the United States is the only country in the world in which helium-bearing natural gases occur in amounts sufficient for helium production. The main supply of helium of military use comes from the U. S. Bureau of Mines, Amarillo Helium Plant in Amarillo, Tex.

Helium is one of the rare gases which make up the earth's atmosphere. It is colorless, odorless, and tasteless. It is remarkable in being extremely inert chemically and physiologically. Its density is one-seventh that of nitrogen and one-eighth that of oxygen and its molecular weight is 4. Helium defuses more rapidly and easily than either nitrogen or oxygen. It is heavier than hydrogen but because it is nonexplosive, it is, of course, much safer and greatly to be preferred to hydrogen for use in lighter-than-air ships. Helium liquifies at 5.2 degrees above absolute zero. Its solubility in water is 0.0083 cc. per cc. of solution while the solubility of nitrogen is 0.0138.

In 1919, Thomson wrote to the Bureau of Mines suggesting the use of helium in deep-sea diving. At that time, he predicted that the maximum depth of dives might be increased by 50 percent or even more. He also made the same suggestion in a letter to McLennan in 1920. These letters were reprinted by Thomson (*2488*) in 1927 and McLennan refers to Thomson's suggestion in a brief report published in 1920.

Sayers, Yant, and Hildebrand (*2513*) in 1925 suggested the use of helium-oxygen mixtures in mitigating the hazards of caisson disease and stated that with such gas mixtures, the time of decompression could be reduced to one-sixth of the ordinary time required. As will be seen from the following discussion, rapid strides were made, from that time on, in our knowledge of the uses of helium in compressed air work and diving by research carried out by collaboration between the U. S. Bureau of Mines and U. S. Navy.

Reference may be made to a note by Yant (*2489*) which appeared in 1927 calling attention to the fact that Cooke applied for a patent on 15 August 1919 the title of which was "atmospheric compound for divers' use." The patent was granted on 6 November 1923 (No. 1, 473, 337) claiming to be a "compound for divers' use comprising oxygen and helium——".

It is suggested that readers wishing to have further information on the physical properties of helium consult a paper by von Antropoff (*2484*) published in 1919. Next to neon, helium is the least soluble of all the known gases and is also remarkable in that its solubility shows little change with alteration in temperature. It is of interest that because of its inertness, helium has been suggested (Stewart (*2487*) 1933) as a preservative for food.

2484. Antropoff, A. von Experimentelle Untersuchung über die Löslichkeit der Edelgase in Flüssigkeiten. *Z. Electrochem.*, 1919, *25:* 269–297.

2485. McLennan, J. C. Helium: its production and uses. *Nature, Lond.*, 1920, *105:* 778–780. [R]

2486. Shilling, C. W. Helium. *Nav. med. Bull., Wash.*, 1941, *39:* 64–71. [M, R, B]

2487. Stewart, A. About helium. *Inform. Circ. U. S. Bur. Min.*, 1933, no. 6745: 1–46. [M, R, B]

2488. Thomson, E. Helium in deep diving. *Science*, 1927, *65:* 36–38. [C, P]

2489. Yant, W. P. Helium in deep diving. *Industr. Engng Chem.*, (News Edition), 1927, *5:* 4–5. [P]

2. PHYSIOLOGICAL EFFECTS OF HELIUM

In a paper published in 1926, Sayers and Yant (*2502*) recalled that many investigators have studied the detrimental effects of high oxygen pressures. These adverse effects include inflammation of the lungs and at the higher pressures, convulsive seizures. Details of the poisonous effects of oxygen under high pressures may be found in the section on oxygen intoxication (p. 163). This action of oxygen at raised pressures limits the use that may be made of high oxygen concentrations by divers and compressed air workers. According to the Hoppe and Bert gas bubble theory of the etiology of decompression sickness, nitrogen is the main component of the gas liberated within the body on decompression. As Sayers and Yant stated, safe decompression from high air pressures requires an excessive amount of time and there is need for a gas that has a lower coefficient of solubility and a greater diffusibility than nitrogen. Helium answers these requirements

and divers may be safely decompressed in shorter times using helium-oxygen mixtures than when diving with ordinary air. However, the greatest advantage of helium-oxygen mixtures for diving appears to consist in its prevention of the mental sluggishness and neuromuscular incoordination occurring at great depths and attributed to nitrogen narcosis.

Sayers and Yant carried out experiments on guinea pigs and white rats in the compression chamber, making parallel runs with helium-oxygen mixtures and nitrogen-oxygen mixtures at pressures of 10 atmospheres. The animals were exposed for periods of 1 to 5 hours and decompressed at varying rates. In the animals breathing helium and oxygen, no bubbles were found after decompressions lasting 15 minutes and no bubbles were found in the animals breathing nitrogen-oxygen mixtures after decompressions lasting 45 minutes. After exposures to helium and oxygen, the animals were active throughout the decompression period and there were no deaths although many of the animals breathing nitrogen-oxygen mixtures died even though decompression was much slower. It was concluded by Sayers and Yant that helium decompression could be carried out with safety in one-third and one-fourth the time required for safe nitrogen decompression and that also there is much less discomfort during decompression with helium. Animal experiments indicated that helium does not exert toxic effects. Four guinea pigs exposed to helium-oxygen mixtures at 10 atmospheres for 1 hour a day on 8 consecutive days exhibited no symptoms when sacrificed and autopsied. Further, rats breathing helium-oxygen mixtures containing 1.5 percent oxygen at 20 atmospheres also suffered no ill effects. The investigators themselves breathed helium-oxygen mixtures for periods up to 2 hours with no noticeable effects except a temporary change in the pitch and quality of the voice.

Experiments of Hershey (*2501*) published in 1930 also suggested that helium-oxygen mixtures are innocuous to animal life. Mice breathing a mixture of 79 percent helium and 21 percent oxygen at normal pressures were unharmed. Hershey concluded from experiments carried out on mice that gas mixtures in which the rare gases were excluded did not support life indefinitely and that the rare gases were essential for life. For example, mice breathing a mixture containing 79 percent nitrogen and 21 percent oxygen, in which the rare gases were excluded, did not live for more than 10 days. Gas mixtures containing more than 70 percent oxygen produced harmful effects and animals breathing pure oxygen died in 2 to 6 days with inflammation and interstitial hemorrhages in the lungs.

Barach (*2490*) in 1934 repeated Hershey's experiments but found that white mice supported mixtures of oxygen and nitrogen (free of rare gases) in normal proportions and lived as long as the experiment was continued (40 days) with no ill effects. There was no change in the oxygen consumption. Barach also determined that rabbits could live unharmed breathing 60 percent oxygen at normal atmospheric pressure for as long as 3 months. Breathing mixtures containing 70 to 80 percent oxygen, some animals showed edema of the lungs; when breathing mixtures containing more than 80 percent oxgyen, all animals showed ill effects.

In 1934–35, Barach (*2491*) pointed out that breathing a mixture of 79 percent helium and 21 percent oxygen required less exertion than breathing air and might, therefore, be useful in the treatment of patients with certain types of respiratory and cardiac diseases. He reported that mice breathing such helium-oxygen mixtures for 2½ months suffered no harmful effects.

Behnke and Yarbrough (*2494*) in 1938 recalled the therapeutic uses of helium and oxygen in asthma and other conditions and its other applications in inhalation anesthesia and diving. Regarding the physiological effects of helium-oxygen mixtures, they called attention to characteristic changes in the voice and the chilling effect during exposure to helium-oxygen mixtures, an effect not yet completely understood. Behnke and Yarbrough stated that "bends" can occur on decompression after helium-oxygen breathing but reported that the more serious effects of decompression,

such as unconsciousness or paralysis, were not encountered. In general, the symptoms were the milder manifestations of decompression sickness such as itching and skin rashes. The pains of the "bends" in these cases were promptly relieved by the recompression treatment. Behnke and Yarbrough attributed this effect of helium and oxygen mixtures to the fact that helium is less soluble and more diffusable than nitrogen and relatively more soluble in tissues that desaturate rapidly whereas a large proportion of the nitrogen goes into solution in tissues which desaturate slowly. It was stated that decompression gave relief more quickly and with lower pressures than were required for "bends" encountered in compressed air. The most striking effect of breathing helium-oxygen mixtures was the feeling of normality experienced by the divers at great depths as opposed to the intoxication and neuromuscular incoordination associated with high air pressures in diving at great depths. Helium-oxygen mixtures were tested up to 16 atmospheres and it was found that the stupefaction and impaired motor control associated with compressed air were abolished or rendered negligible. At 500 ft., a diver felt well and happy, and thought he was only at a depth of 100 ft. When the helium-oxygen mixture was replaced by air at 300 ft., the diver felt dizzy, lost motor control, and demanded to be brought to the surface.

Comparison between performance in diving tests made under compressed air and under compressed helium-oxygen mixtures showed that speed and accuracy were both enhanced under the latter conditions. Divers breathed helium-oxygen mixtures for periods averaging 3½ hours at different pressures. The helium content of the body and rate of helium elimination were then det.rmined and it was found that the time required for helium elimination was about one-third to one-half that for nitrogen elimination. One diver breathing helium-oxygen mixtures was 56.5 percent desaturated from helium 20 minutes after cessation of helium inhalation, and 99.5 percent desaturated in 330 minutes.

Further experiments by Behnke and Yarbrough (*2495*) published in 1939 showed that the average resistance to gas flow for a mixture of 80 percent helium and 20 percent oxygen was less than for air or a mixture of 86 percent argon and 14 percent nitrogen. Helium was found to be much less soluble in olive oil or water than either argon or nitrogen.

Regarding the mental effects of breathing argon-oxygen mixtures, Behnke and Yarbrough found a greater depressant effect from a 69 percent argon, 11 percent nitrogen, and 20 percent oxygen mixture than from air. A diver breathing this mixture at 130 ft. thought he was at 200 ft.; at 90 ft., he believed that he was at 150 ft.; and at 120 ft., another diver thought that he was at 250 ft. Substitution of air for the argon mixture without telling the subject led to a clearing of the mental fogginess. At a pressure of 1 atmosphere, no physiological differences could be detected between oxygen mixtures containing argon, nitrogen, and helium, respectively.

A further report by Behnke (*2493*) in 1940 stated that nitrogen absorption and elimination and ether absorption and elimination have similar rates. Helium is absorbed and eliminated more rapidly than nitrogen. The depressant effects on neuromuscular activity produced by nitrogen and argon were again referred to and it was stated that argon is more depressant than nitrogen. The substitution of helium minimizes or eliminates this depression. According to the Meyer-Overton hypothesis, the narcotic effect of a foreign substance is proportional to its solubility in lipoid tissue. The results reported by Behnke appear to confirm this hypothesis. With regard to electroencephalographic changes resulting from high pressures, it was noted that while high air pressure causes a decrease in the alpha waves, there was no such decrease when helium-oxygen mixtures were breathed. The voice changes, characterized by a rise in pitch and a nasal quality, were commented on. These voice changes persist even when a helium-oxygen atmosphere is compressed. This may render telephone communication with deep-sea divers difficult. Regarding the chilling effect of breathing helium-oxygen mixtures, it was found that twice as much heat must be supplied to a diver sur-

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rounded by a helium-oxygen mixture (in an electrically heated suit) as compared to breathing air.

According to Dublin, Baldes, and Williams (*2499*) 1940, the voice changes resulting from breathing helium-oxygen mixtures are caused by variations in the overtones. It is claimed that the fundamental vibrations are unchanged. Helium-oxygen mixtures are stated to impede the vocal cords less than air so that the velocity of sound is increased and the sound pattern of resonanting cavities of the nasopharyngeal passage is changed.

Regarding the effect of helium-oxgyen inhalation on the kinetics of lung ventilation, Dean and Visscher (*2497*) 1941 concluded, on the basis of experiments on curarized dogs, that the viscous resistance of normal lungs is not changed when a helium-oxygen mixture is substituted for air. However, the viscous resistance produced by obstruction which causes turbulence is reduced by substitution of a helium-oxygen mixture for air. It was stated that helium acts in reducing the work of ventilation by a reduction of turbulence in gas flow.

Dill, Edwards, and McFarland (*2498*) 1935–37 measured the respiratory responses of 5 subjects breathing an 80 percent helium and 20 percent oxygen mixture compared with the same subjects breathing air. There was a 10 percent increase in ventilation when the helium mixture was breathed but no increase in oxygen consumption. It was concluded, therefore, that the capacity of normal men to transport oxygen to working muscles was not improved by reducing the density of the inspired air. On the other hand, it does appear quite clear that oxygenation may be improved by breathing helium-oxygen mixtures in cases of asthma and other forms of respiratory obstruction.

2490. Barach, A. L. Rare gases not essential to life. *Science*, 1934, N. Ser., *80:* 593–594. [P]

2491. Barach, A. L. Use of helium as a new therapeutic gas. *Proc. Soc. exp. Biol; N. Y.*, 1934–35, *32:* 462–464. [P]

2492. Barach, A. L. and M. Eckman. The use of helium as a new therapeutic gas. *Curr. Res. Anesth.*, 1935, *14:* 210–215. [P]

2493. Behnke, A. R. Some physiological considerations of inhalation anesthesia and helium. *Curr. Res Anesth.*, 1940, *19:* 35–41. [P]

2494. Behnke, A. R. and O. D. Yarbrough. Physiologic studies of helium. *Nav. med. Bull., Wash.*, 1938, *36:* 542–558. [P]

2495. Behnke, A. R. and O. D. Yarbrough. Respiratory resistance, oil-water solubility, and mental effects of argon, compared with helium and nitrogen. *Amer. J. Physiol.*, 1939, *126:* 409–415. [P]

2496. Cohn, R. and S. Katzenelbogen. Electroencephalographic studies. *Nav. med. Bull., Wash.*, 1939, *37:* 596–599. [P]

2497. Dean, R. B. and M. B. Visscher. The kinetics of lung ventilation. An evaluation of the viscous and elastic resistance to lung ventilation with particular reference to the effects of turbulence and the therapeutic use of helium. *Amer. J. Physiol.*, 1941, *134:* 450–468. [P]

2498. Dill, D. B., H. T. Edwards, and R. A. McFarland. Respiratory responses to changes in air density. *Arbeitsphysiologie*, 1935–37, *9:* 341–344. [P]

2499. Dublin, W. B., E. J. Baldes, and M. M. D. Williams. Voice changes with a mixture of helium and oxygen. *Proc. Mayo Clin.*, 1940, *15:* 586–588. [P]

2500. Hershey, J. W. Physiological effects of oxygen atmospheres diluted by nitrogen. *Trans. Kans. Acad. Sci.*, 1929, *32:* 51–52. [P]

2501. Hershey, J. W. Components of air in relation to animal life. *Science*, 1930, *71:* 394–396. [P]

2502. Sayers, R. R. and W. P. Yant. The value of helium-oxygen atmosphere in diving and caisson operations. *Curr. Res. Anesth.*, 1926, *5:* 127–138. [P]

2503. Anon. Helium-oxygen mixture in diving. *Nav. med. Bull., Wash.*, 1927, *25:* 154. [P]

2504. Anon. Voice changes from inhalation of helium-oxygen. *J. Amer. med. Ass.*, 1939, *113:* 706. [P]

3. TECHNIQUE OF USE OF HELIUM

In 1927, Thomson (*2511*) recommended that helium-oxygen mixtures for divers could be recirculated through a filter to remove "impurities and effete gases" and renew the oxygen content, thus preventing wastage of helium. In 1938, Lovelace (*2509*) used the B. L. B. mask for administration of helium-oxygen mixtures to patients. Treatment was started with 80 percent helium-20 percent oxygen mixtures, the amount of oxygen being increased as the patient's condition improved. The rate of flow could be adjusted to suit individual needs. In 1939, Eckman and Barach (*2508*) described apparatus and techniques for administering oxygen and helium-oxygen mix-

tures. The use of basal metabolism apparatus for recirculating helium and preventing its loss was recommended by Matzger (*2510*) in 1939. This author also recommended an 80 percent helium-20 percent oxygen mixture for promoting expectoration. New apparatus for the administration of helium-oxygen mixtures was described in 1940 by Brubach, Crisp, and Neal (*2506*). For a description of a method of analysis of mixtures of helium, oxygen, and nitrogen by determination of the velocity of sound, the reader is referred to a paper by Dublin, Boothby, Brown, and Williams published in 1940.

2505. Benedict, F. G., P. White, and R. C. Lee. An infant incubator employing controlled mixtures of helium and oxygen to combat respiratory failure. *Amer. J. Obstet. Gynec.*, 1940, *39:* 63–70.

2506. Brubach, H. F., L. R. Crisp, and P. A. Neal. A new apparatus for the administration of helium-oxygen mixtures. *Publ. Hlth Rep., Wash.*, 1940, *55:* 1776–1782. [P]

2507. Dublin, W. B., W. M. Boothby, H. O. Brown, and M. M. D. Williams. Analysis of mixtures of helium, oxygen and nitrogen by means of determination of the velocity of sound: further observations. *Proc. Mayo Clin.*, 1940, *15:* 412–416. [P]

2508. Eckman, M. and A. L. Barach. Inhalational therapy equipment. *Mod. Hosp.*, 1939, *52:* 78–84. [P]

2509. Lovelace, W. R., II. Technic of treatment with helium and oxygen using B. L. B. inhalation apparatus. *Proc. Mayo Clin.*, 1938, *13:* 790–791. [P]

2510. Matzger, E. Helium and oxygen mixture. *Calif. West. Med.*, 1939, *50:* 418–419. [P]

2511. Thomson, E. Helium. *Science*, 1927, *65:* 299–300. [P]

4. GENERAL STUDIES OF USES OF HELIUM-OXYGEN MIXTURES

In addition to Shilling's report on helium (*2486*) which appeared in 1941, reference may be made to a paper published in 1925 by Sayers, Yant, and Hildebrand (*2513*) on the use of helium-oxygen mixtures in the prevention of caisson disease. The authors believe that helium-oxygen mixtures, if substituted for air in diving work, will reduce the time of decompression. In animal experiments with helium-oxygen mixtures, the decompression time was as low as one-sixth of the time required with air and in a few preliminary trials on human subjects, decompression was safely accomplished in approximately one-fourth the time recommended with air. It was stated that helium-oxygen mixtures were apparently without deleterious effects on the body. Guinea pigs exposed to such mixtures on two to four occasions for periods of 1 to 3 hours at 10 atmospheres within a period of 3 to 7 days and then sacrificed, showed some bubbles in a few cases but were otherwise apparently normal. Four guinea pigs were subjected on 8 consecutive days to a helium-oxygen mixture at 10 atmospheres for 1 hour and decompressed at a rate of 25 minutes. For 4 weeks, there was no apparent pathological effect nor were there any symptoms.

A brief article by Clough (*2512*) 1939 lists several uses of helium-oxygen mixtures. It was suggested that helium-oxygen atmospheres be used for caisson workers and for divers. Helium-oxygen mixtures were stated to prevent bubble formation and also to lessen the pains of oxygen poisoning. Helium-oxygen mixtures were also believed to have a useful place in the treatment of obstructive lesions in the respiratory tract since such gas mixtures required less effort for effective breathing. Helium may also be added to inhalation anesthetic mixtures, especially for patients with respiratory obstructions.

2512. Clough, G. M. The use of helium. *Med. J. Aust.*, 1939, *2:* 400–402. [R]

2513. Sayers, R. R., W. P. Yant, and J. H. Hildebrand. Possibilities in the use of helium-oxygen mixtures as a mitigation of caisson disease. *Rep. Invest. U. S. Bur. Min.*, 1925, no. 2670: 1–15. [R]

2514. Wickner, I. Combined helium and epinephrine therapy. *Ann. Allergy*, 1945, *3:* 187–190, 206.

5. USE OF HELIUM-OXYGEN MIXTURES IN RESPIRATORY DISEASES

The effects of helium-oxygen inhalation on the mechanics of respiration were reported by Barach and Eckman (*2520*) in 1936. These investigators simulated obstructive conditions in the respiratory tract by making normal individuals breathe through a constricted orifice. On inhaling air or 100 percent oxygen, the air pressure in the trachea was increased, the respiratory rate slowed, and the tidal volume increased. Substitution of an 80 percent helium-20 percent oxygen mixture

reduced the tracheal pressure, increased the respiratory rate to normal, decreased the tidal volume, and partially relieved the symptoms of dyspnea. Similar results were obtained on experiments with dogs. With regard to the percentage of helium and of oxygen in the mixtures, it was found that 30 to 35 percent oxygen with 65 to 70 percent helium seemed better than any other combination. In 1935, Barach (*2515*) reported striking results in the alleviation of asthma by inhalation of oxygen-helium mixtures in an oxygen tent or with a face mask from a Douglas bag. Helium-oxygen mixtures also relieved cyanosis and dyspnea in obstructive lesions in the trachea and larynx. Four case histories describing the use of helium-oxygen mixtures in asthma were given. A similar report was published in 1935 by Barach and Eckman (*2519*).

Three cases of severe intractable asthma were relieved by inhalation of a 70 percent helium-30 percent oxygen mixture in the oxygen tent. In the report of these cases by Maytum, Prickman, and Boothby in 1935 (*2527*), it was noted that one patient inhaled the mixture continuously for 24 hours and at intervals of 3 days thereafter without any ill effects.

Other reports on the therapeutic use of helium and oxygen in the treatment of asthma are those by Barach (*2516*, *2517*) 1936. In the first of these articles, Barach pointed out that helium-oxygen mixtures are of value in the treatment of severe asthma of the type refractory to epinephrine and wherever obstructive dyspnea accompanies the condition. In some instances, this form of therapy makes it possible to avoid tracheotomy. It appears also that helium-oxygen mixtures may be useful in easing the discomfort and dyspnea of severe emphysema.

Kernan and Barach (*2525*) in 1937 also called attention to the use of helium in cases of obstructive lesions in the trachea and larnyx and in 1938, Barach described physiological methods in the diagnosis and treatment of asthma and emphysema involving the use of helium-oxygen mixtures in a rebreathing apparatus or in a tent. In 1938, Maytum pointed out that helium-oxygen mixtures were useful in relieving cyanosis in severe intractable asthma although there was little effect on the dyspnea. It was recommended that after relief by helium-oxygen mixtures, the patient be given epinephrine for more lasting results.

Case histories describing the use of helium-oxygen mixtures in patients with asthma and stridor were given in 1939 by Boothby, Mayo, and Lovelace (*2521*). In 1939, Metz, Wearner, and Evans (*2528*) described the use of helium-oxygen mixtures in the treatment of status asthmaticus, obstructive breathing, and post-operative atelectasis. Helium administration was also recommended by Vollbrechthausen (*2532*, *2533*) in 1939 for glottal spasm, edema of the glottis, compression of the trachea, cases with insufficient amplitude of the respiratory movements, and prolonged anesthesia.

Boothby, Mayo, and Lovelace (*2522*) in 1940 recommended the use of helium-oxygen mixtures in any case of respiratory obstruction before resorting to tracheotomy. This article contains an excellent account of the historical development of the use of oxygen and of helium-oxygen mixtures in compressed air workers and for other therapeutic purposes. The authors reported administering 100 percent oxygen to 1,800 patients with no sign of pulmonary irritation although some patients received oxygen continuously for 48 hours. Methods of administration were considered.

The therapeutic use of helium-oxygen mixtures to interrupt the cycle of status asthmaticus was mentioned by Eyermann (*2523*) in 1940, and Sollmann (*2531*) 1942 also referred to the use of a 79 percent helium-21 percent oxygen mixture for relieving obstructive dyspnea and in post-operative tracheal edema, hemorrhage, and laryngospasm. In 1940, Kane (*2524*) reported on the use of an 80 percent helium-20 percent oxygen mixture in the relief and treatment of asphyxia neonatorum in 200 babies. Two reports concerning the use of helium in the management of pneumothorax may be consulted. The first is that of Reinders (*2529*) 1930, the second that of Schedtler (*2530*) published in 1938. The latter

author stated that since helium escaped almost as fast as air from an artificial pneumothorax in the treatment of tuberculosis there was no reason for using this gas in preference to air.

2515. Barach, A. L. The use of helium in the treatment of asthma and obstructive lesions in the larynx and trachea. *Ann. intern. Med.*, 1935, *9*(1): 739–765. [R]

2516. Barach, A. L. Gas therapy. *Amer. J. Surg.*, 1936, N. Ser., *34:* 588–590. [P, R]

2517. Barach, A. L. The therapeutic use of helium. *J. Amer. med. Ass.*, 1936, *107:* 1273–1279. [P, R]

2518. Barach, A. L. Physiological methods in the diagnosis and treatment of asthma and emphysema. *Ann. intern. Med.*, 1938, *12:* 454–481. [P]

2519. Barach, A. L. and M. Eckman. The use of helium as a new therapeutic gas. *Curr. Res. Anesth.*, 1935, *14:* 210–215. [P]

2520. Barach, A. L. and M. Eckman. The effects of inhalation of helium mixed with oxygen on the mechanics of respiration. *J. clin. Invest.*, 1936, *15:* 47–61. [P]

2521. Boothby, W. M., C. W. Mayo, and W. R. Lovelace, II. Oxygen, and oxygen and helium therapy: recent advances. *Med. Clin. N. Amer.*, 1939, *23:* 977–1005. [R]

2522. Boothby, W. M., C. W. Mayo, and W. R. Lovelace, II. The use of oxygen and oxygen-helium, with special reference to surgery. *Surg. Clin. N. Amer.*, 1940, *20:* 1107–1168. [R]

2523. Eyermann, C. H. Diagnosis and treatment of bronchial asthma. *Dis. Chest*, 1940, *6:* 234–239.

2524. Kane, H. F. The use of helium and oxygen in the treatment of asphyxia neonatorum. Preliminary communication. *Amer. J. Obstet. Gynec.*, 1940, *40:* 140–141. [P, Ch]

2525. Kernan, J. D. and A. L. Barach. Rôle of helium in cases of obstructive lesions in the trachea and larynx. *Arch. Otolaryng., Chicago*, 1937, *26:* 419–447. [P]

2526. Maytum, C. K. Helium and oxygen treatment of intractable asthma. *Proc. Mayo Clin.*, 1938, *13:* 788–789. [P]

2527. Maytum, C. K., L. E. Prickman, and W. M. Boothby. The use of helium and oxygen in the treatment of severe intractable asthma. *Proc. Mayo Clin.*, 1935, *10:* 788–790. [P]

2528. Metz, C. W., A. A. Wearner, and A. E. Evans· The therapeutic use of helium. *Sth. med. J., Birmingham*, 1939, *32:* 34–40. [R]

2529. Reinders, [ ]. Helium bij de pneumothorax-behandeling. *Ned. Tijdschr. Geneesk.*, 1930, *74:* 6112. [P]

2530. Schedtler, [ ]. Über die Verwendbarkeit des Heliums zur Pneumothoraxfüllung. *Klin. Wschr.*, 1938, *17:* 1153–1154. [P]

2531. Sollmann, Torald. *A manual of pharmacology and its applications to therapeutics and toxicology.* Philadelphia, W. B. Saunders Company, 1942, x, 1298 pp. [R]

2532. Vollbrechthausen, F. El gas helium en anestesiologia. *Arch. med. ferroc.*, 1939, *1:* 159–165.

2533. Vollbrechthausen, F. Primeras administraciones del gas helium en Mexico. *Rev. mex. Cirug. Ginec. Cánc.*, 1939, *7:* 9–16.

2534. Anon. Breathing helium brings relief to asthma sufferers. *Sci. News Lett., Wash.*, 1935, *27:* 318.

6. USE OF HELIUM-OXYGEN MIXTURES IN INHALATION ANESTHESIA

The use of helium as a component in the gas mixtures compounded for purposes of inhalation anesthesia has been recommended by a number of authors. Sykes and Lawrence (*2538*) in 1938 found that helium-oxygen mixtures could be breathed through an artificial obstruction twice as long as air before exhaustion occurred. This greater ease of respiration with helium-oxygen mixtures suggested the use of helium in anesthetic mixtures in cases of partial obstruction during the administration of inhalation anesthesia. Eversole (*2536*) 1938 used helium for the relief of stridor and partial obstruction during inhalation anesthesia. Mixtures of helium-oxygen and cyclopropane were used. Out of 105 cases, 55 cr 52.4 percent obtained complete relief; 37 or 35.2 percent obtained partial relief; and 13 or 12.4 percent were unrelieved. Eversole pointed out the necessity of careful attention to the prevention of anoxia.

In 1939, Bonham (*2535*) reported on his experiences with the use of helium in inhalation anesthesia mixtures in 175 cases. He gave three case histories in detail. Approximately 15 percent of his cases failed to benefit from helium administration while the remainder were definitely helped. Bonham pointed out that helium dilutes a cyclopropane-oxygen mixture, making it lighter and more volatile and rendering breathing easier. Moreover, helium is inert and nonexplosive. Also he considered that the presence of helium in the mixture permits other gases to be carried to the alveoli more easily. Bonham believed that helium should be used at the end of anesthesia to wash out excess cyclopropane.

The question of inflammability of ether-oxygen-helium mixtures has been examined by Jones, Kennedy, and Thomas (*2537*) 1941. Their experiences show that the oxygen con-

tent of such mixtures must be kept below approximately 16 percent (in the range of mixtures usually employed in anesthesia) in order to eliminate explosion hazards. Strictly noninflammable mixtures are, therefore, not entirely practical. However, ether-oxygen-helium mixtures were compounded in which a flame was propagated slowly through the test apparatus but no explosion of any violence was produced. Under certain circumstances, such mixtures in which the inflammability is of a mild order may be advantageous. These mixtures are definitely safer from an explosion standpoint than those with a high percentage of oxygen.

2535. Bonham, R. F. The value of helium as an adjunct in general anesthesia. *Curr. Res. Anesth.*, 1939, *18:* 54–57. [R]

2536. Eversole, U. H. The use of helium in anesthesia. *J. Amer. med. Ass.*, 1938, *110:* 878–880. [R]

2537. Jones, G. W., R. E. Kennedy, and G. J. Thomas. Inflammability of ether-oxygen-helium mixtures: their application in anesthesia. *Rep. Invest. U. S. Bur. Min.*, 1941, no. 3589, 1–15. [P, R]

2538. Sykes, W. S. and R. C. Lawrence. Helium in anaesthesia. *Brit. med. J.*, 1938, *2:* 448–449. [R]

7. USE OF HELIUM-OXYGEN MIXTURES IN AEROTITIS MEDIA

Reference has been made in the section on ear, nose, and throat disturbances (p. 94) to aerotitis media as a condition arising from failure of equalization of pressure in the middle ear. Because of the structural characteristics of the pharyngeal opening of the Eustachian tube, blockage of the passage of air through the tube is more likely to occur during compression than during decompression. Lovelace, Mayo, and Boothby (*2541*) in 1939 suggested that helium, on account of its greater rate of diffusion, would speed equalization of pressure and so prevent ear blocking and trauma. Helium-oxygen mixtures were tried on several airplane flights either during descent or after landing to relieve symptoms. Favorable results were obtained in 15 out of 16 cases.

The use of helium-oxygen mixtures for the alleviation of tubal and sinus blockage in compressed air workers was discussed in 1940 by Cross n, Jones, and Sayers (*2539*). This report contains a brief historical resumé of the use of helium in compressed air work and describes various degrees of severity of aerotitis media. According to these authors, there may be cases in which the ears are not involved but rather the accessory nasal sinuses. They claim that if the "blocked" worker returns to normal pressure, thus easing the block, and then breathes a helium-oxygen mixture, the passages are more likely to remain open on subsequent compression. The U. S. Bureau of Mines laboratories designed a simple apparatus which could be placed in the man lock so that "blocked" caisson workers could breathe helium-oxygen mixtures. Eighty two out of eighty-four cases reacted favorably to this treatment. However, the treatment was not effective if the "block" was complicated by inflammation.

In 1940, Hall (*2540*) reported on the use of helium-oxygen mixtures in aviation for the prevention of painful ear symptoms. Twenty subjects were brought from 10,000 ft. to sea level first breathing air and then 80 percent helium-20 percent oxygen mixtures. The subjects were not allowed to clear the ears voluntarily so that block was produced. Ear pain developed in all cases with air or helium-oxygen mixtures although there was some indication that slightly greater barometric pressure changes were necessary to cause the different degrees of pain when helium-oxygen mixtures were breathed. It appeared that the rate of descent had no noticeable effect upon the incidence of symptoms.

In 1941, Requarth (*2542*) described the treatment of 400 cases of aerotitis media in compressed air workers on the Chicago subway system tunnels. One-half of these were treated with helium-oxygen mixtures and the other half were not. The nasopharyngeal passages were sprayed with a 2 percent solution of ephedrine sulfate in physiological saline preparatory to administration of the helium-oxygen mixture. A mixture of 80 percent helium and 20 percent oxygen was breathed from the B. L. B. mask or Politzer bag. Treatments were begun as soon as the patient left the lock. Of 200 cases treated with the helium-oxygen mixture, 52 obtained no

relief, 38 gained moderate relief, and 110 were completely relieved. Only 1.5 percent of those treated with the helium-oxygen mixture developed suppurative aerotitis media as compared with 4.5 percent of the untreated cases. The inhalation of the helium-oxygen mixture was of no value when the middle ear was filled with fluid.

A report of the treatment of ear-block caused by changes in atmospheric pressure was given in 1943 by Thorne (*2544*) who was in charge of the medical station in the building of a dry dock at the Norfolk Navy Yard. The work was carried out on a 24-hour schedule under conditions of inclement weather. Upper respiratory infections were common and there was a large number of cases of ear-block. All workers experiencing block were "locked out" immediately and sent to the medical station for treatment. After having been treated, they were tested in the medical lock up to a pressure of 10 lb. per sq. in. If the ears remained clear, workers were sent back to work. If they became blocked again, they were assigned to sick quarters. One-half the cases were treated with an 80 percent helium-20 percent oxygen mixture, inhaling the gas for 3 to 5 minutes. The other half were treated with 0.5 percent neosynephrine hydrochloride, 10 drops in each nostril. With the helium-oxygen treatment, Thorne reported 141 cures and 12 failures, while with the neosynephrine treatment, there were 64 cures and 89 failures. Thorne considered that the mode of action of the helium-oxygen mixture was still not understood. He recalled that its action had been attributed to more rapid equalization of pressure because of the greater diffusibility of helium gas. The author suggested that helium might have some direct action on the mucous membrane of the upper respiratory tract.

For further reference to the use of helium-oxygen mixtures in ear block, the reader is referred to Singstad's report (*2543*) which appeared in 1944.

2539. Crosson, J. W., R. R. Jones, and R. R. Sayers. Helium-oxygen mixtures for alleviation of tubal and sinus block in compressed air workers. *Publ. Hlth Rep., Wash.*, 1940, *55:* 1487–1496. [P, R]

2540. Hall, J. F., Jr. The use of helium-oxygen mixtures in aviation for the prevention of painful ear symptoms. *J. Aviat. Med.*, 1940, *11:* 81–86. [P, R]

2541. Lovelace, W. R., II, C. W. Mayo, and W. M. Boothby. Aero-otitis media: its alleviation or prevention by the inhalation of helium and oxygen. *Proc. Mayo Clin.*, 1939, *14:* 91–96. [P, R]

2542. Requarth, W. H. Aero-otitis media in compressed air workers. Treatment with helium-oxygen mixtures. *J. Amer. med. Ass.*, 1941, *116:* 1766–1769. [P, R]

2543. Singstad, O. The Queens midtown tunnel. Discussion. *Proc. Amer. Soc. civil Engrs.*, 1944, *70:* 375–386. [R]

2544. Thorne, I. J. The administration of helium and oxygen mixtures in the treatment of disabling ear symptoms caused by changes in atmospheric pressure. *Nav. med. Bull., Wash.*, 1943, *41:* 378–385. [P, R]

8. USE OF HELIUM-OXYGEN MIXTURES IN DIVING

In 1937, End (*2547*) reported experiments carried out on human subjects to determine decompression times with various gas mixtures containing helium. Tests were carried out in a steel compression chamber and the subjects were kept at a pressure equivalent to 90 ft. depth for 1 hour. Three runs were carried out with three different gas mixtures as follows:

Experiment number	Oxygen percentage	Nitrogen percentage	Helium percentage
I	21	52.5	26.5
II	21	26.5	52.5
III	21	0	79.0

In experiment I, subjects tolerated a total decompression time of 8 minutes; in experiment II, the decompression time was 4 minutes; while in experiment III, return to normal pressure occupied only 2 minutes. No ill effects were observed by any subjects and there were no symptoms except a change in the pitch and quality of the voice.

In 1938, End (*2548*) described the use of helium gas in a world's record dive. The suit used was designed by Nohl and was of the self-contained type with gas cylinders on the back. On 1 December 1937 Nohl, using a helium-oxygen mixture, reached a depth of 420 ft. in Lake Michigan near Port Washing-

ton, Wisc. without any alteration in mental state or any subsequent ill effects from the dive. The following schedule of this dive is of interest:

1250—entered water.
1251—100 ft.
1252—165 ft.
1253—200 ft.
1319—240 ft.; began ascent, line fouled.
1323—surfaced.
1325—re-entered water.
1334—420 ft. on bottom.
1343—began ascent.
1355—200 ft.
1405—30 ft.
1427—20 ft.
1455—10 ft.
1541—surfaced.

In 1939, Ellsberg (*2546*) stated that Momsen using helium-oxygen mixtures, took divers to pressures corresponding to depths of 500 ft. below sea level in the experimental diving tank at the Experimental Diving Unit, Navy Yard, Washington, D. C.

An account was given in 1942 by Behnke (*2545*) of 2 dives made to the sunken U. S. S. *Conger* (*O–9*) on 22 June 1941 at a depth of 440 ft. using a mixture of helium and oxygen. The divers felt well at this depth (approximately 210 lb. per sq. in.) and remained at the bottom for 10 minutes. Decompression from 440 ft. to 170 ft. was carried out in 3 minutes with a stage of 7 minutes at 170 ft. Two-minute stops were made at 120 ft. and 110 ft.; 3-minute stops at 100 ft. and 90 ft.; a 6-minute stop at 80 ft.; a 9-minute stop at 70 ft.; and a 10-minute stop at the 60 ft. level, at which point the helium-oxygen mixture was replaced by pure oxygen. A 10-minute stop was made at 20 ft. The divers were then brought to the surface and decompression was completed by the inhalation of oxygen for a period of 70 minutes from a pressure level corresponding to 50 ft. Regarding comparative decompression times for helium-oxygen mixtures and air dives, Behnke considered that for short exposures up to 30 minutes' duration, the decompression time is approximately the same for both. For longer exposures, during which the body fat becomes saturated with the particular gas mixture, the decompression time may be reduced to about one-third or even less for helium as compared with air. The lessened incidence of "bends," following long exposures in compressed helium atmospheres, was ascribed to the comparatively low solubility of helium in fat. It is also predicted that helium-oxygen atmospheres should minimize the tendency to spinal cord injury in divers since the spinal cord substance contains a high percentage of myelin. Behnke's report also refers to surface decompression and the selection of divers resistant to "bends." It was found that resistance to decompression to simulated high altitudes was correlated with resistance to "bends" in diving. The divers selected to make the 440 ft. dives were those who had been able to ascend to a simulated altitude of 40,000 ft. at a rate of 5,000 ft. per minute and to remain at this altitude for 1 hour without symptoms of decompression sickness.

2545. Behnke, A. R., Jr. Employment of helium in diving to new depths of 440 feet. *Nav. med. Bull., Wash.*, 1942, *40:* 65–67. [P, R]

2546. Ellsberg, E. Diving gas. *Collier's*, 1939, *103* (15): 22; 26; 28. [R]

2547. End, E. Rapid decompression following inhalation of helium-oxygen mixtures under pressure. *Amer. J. Physiol.*, 1937, *120:* 712–718. [P, R]

2548. End, E. The use of new equipment and helium gas in a world record dive. *J. industr. Hyg.*, 1938, *20:* 511–520. [P, R]

XII. DIET AND PHYSICAL FITNESS

Diet and oral hygiene are of paramount importance in the maintenance of submarine crews. However, the literature on this subject is scanty. Papers by Green (*2550*) 1925, Adams (*2549*) 1930, and Scherstén (*2555*) 1940 may be consulted. In regard to physical fitness, a series of papers by the following authors may be referred to: Wilce (*2557*) 1945, Lull (2553) 1945, Little (*2552*) 1945, McMeel (*2554*) 1945, Hahn (*2551*) 1945, and Wells (*2556*) 1945. The installation of refrigerators aboard submarines has permitted a diet consisting of fresh fruits and vegetables. If fresh foods are not available, vitamins should be supplied in concentrated form. The importance of a good cook on the submarine is well recognized. Submarine crews on long

patrols show a reduced exercise tolerance for a short period on returning to their base. Adequate rest periods between patrols are essential in the maintenance of the health of personnel.

2549. Adams, B. H. An improvement in the diet for submarine crews. *Nav. med. Bull., Wash.*, 1930, *28:* 744–745. [R]

2550. Green, R. C. The importance of oral hygiene to submarine personnel. *Nav. med. Bull., Wash.*, 1925, *22:* 447–448. [R]

2551. Hahn, E. V. Physical fitness from a psychiatric standpoint. *J. Indiana med. Ass.*, 1945, *38:* 89–90.

2552. Little, W. D. General considerations of the physical fitness problem. *J. Indiana med. Ass.*, 1945, *38:* 84–86.

2553. Lull, G. F. Fitness for duty of military patients on discharge from hospital. *J. Indiana med. Ass.*, 1945, *38:* 82–83.

2554. McMeel, J. E. Physical fitness. *J. Indiana med. Ass.*, 1945, *38:* 87–88.

2555. Scherstén, B. Angående vitaminhalten i standardstater för Ub vid konservutspisning. *Tidskr. milit. Hälsov.*, 1940, *65:* 49–59.

2556. Wells, C. R. A message on physical fitness. *J. Indiana med. Ass.*, 1945, *38:* 107–108.

2557. Wilce, J. W. A medical viewpoint on national fitness. *J. Indiana med. Ass.*, 1945, *38:* 77–80.

XIII. SANITARY FACILITIES

In times past, constipation has been regarded as almost an occupational disease of submarine personnel because of inadequate toilet facilities. Bouquet (*2558*) 1918–19 and many others have recommended better toilet installations. On modern submarines, toilet and bath facilities are greatly improved.

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Therapeutic Effects of Gases Under Raised Atmospheric Pressures and Respiration of Compressed and Rarefied Air

I. THERAPY WITH PRESSURE CHAMBERS

A. HISTORY OF THE THERAPEUTIC ACTION OF GASES UNDER PRESSURE

Soon after the design and construction by Triger (*77*) in 1841 of the caisson, and with the increasing number of underwater operations employing air under high atmospheric pressures, untoward effects on workers in compressed air began to be reported. During compression, there was pain due to failure of ventilation of the middle ear as well as certain symptoms on decompression which constitute the clinical entity known as caisson disease. Not only were adverse symptoms noted but also high pressure air seemed to exert certain favorable effects on the functions of the human body both in health and in disease. For example, a number of cases were reported in which individuals suffering from catarrhal deafness appeared to hear better in the caisson, and many workers claimed to have a feeling of well-being and heightened muscular power while under pressure. Climbing the ladder to the lock was accomplished with apparently little exertion.

The possible therapeutic value of air under pressure and the indications for this form of therapy occupied the attention of many experimenters and clinicians in the nineteenth century, and since these investigations have contributed, to some extent, to our knowledge of the physiological and pathological effects of raised atmospheric pressures and since they also form an integral part of the history of the subject, an analysis of this literature appears justified.

Serious scientific interest in the pressure and weight of the air goes back to the 17th century. Galileo (see *3*) knew that the air had weight and that the resistance to a vacuum could be measured by the height of a water column. He observed also that at sea level a pump will not suck water to a level higher than 32 ft. In 1643, Torricelli (*2589, published in 1715*) investigated this resistance to a vacuum by the use of a vertical column of mercury which he found required one-fourteenth the length of the corresponding water column. Such a column of mercury within a tube, closed at the top, constituted the first barometer and Pascal (*2579*) 1664 discovered by experiment that the height of the column was approximately 3 inches lower on the Puy de Dôme, a high mountain in Auvergne, than at sea level in Paris.

The most significant early landmark in the history of the physiology of air under varying pressure is the work of Robert Boyle who made his first air pump in 1659 with the aid of Robert Hooke. From that time until his death, nearly 30 years later, Boyle continued to investigate the properties of atmospheric air. Boyle (*2562*) 1666 gave the first reasonable explanation of the barometer and studied and

described with minute accuracy the behavior of various animals in a decompression chamber (*2561*, *2562*, *2563*, *2564*, *2565*, *2566*, *2567*) 1660 to 1682. Boyle's description (*2565*) 1670 of an air bubble in the eye of a viper subjected to decompression constitutes the first recorded description of the phenomenon of aeroembolism.

The first suggestion that raised or lowered air pressures might be used in the treatment of human illness was made in 1664 by Henshaw in England who proposed the construction of an airtight room or "domicillium" in which suitable climatic and pressure conditions could be produced. (See Simpson (*2609*) 1857.) This chamber, as designed by Henshaw, was a square structure in which the air pressure could be raised to levels above 1 atmosphere or decompressed to levels below 1 atmosphere. A barometer was fixed in the room and provisions were made for ventilation. It was proposed that acute diseases be treated by allowing patients to remain for considerable periods in compressed air, whereas, in chronic diseases the subject was to be given repeated 2- to 3-hour sessions during which the pressure was lowered to levels less than 1 atmosphere. In the chill or shivering stage of a fever, decompression was recommended, while in the "hot" stage, compression was suggested as the procedure of choice.

No account appears in the literature of any application of Henshaw's treatment and nothing further was heard of the method until in 1783 the Haarlem Academy of Science offered a prize for the description of an apparatus for compressing the air and for studies with this apparatus on the effects of compressed air on the human organism, animal life, growth of plants, and the combustability of various gases. This prize apparently was never awarded and although, through the experiences of divers and workers in diving bells, knowledge of the effects of high atmospheric pressure continued to accumulate, this knowledge was not extended to possible therapeutic applications.

A considerable impetus, however, was provided by the far-reaching investigations of Lavoisier and Priestley which were followed by a widespread interest in the possible clinical uses of oxygen and other newly discovered gases. At Bristol, England, there was established, in the early part of the nineteenth century under the direction of Beddoes, professor of chemistry at Oxford, a pneumatic institute for the study of the effects of gases and gas mixtures in the treatment of disease. A large number of diseases and symptoms were considered from the point of view of their amenability to this new form of pneumatotherapy, among them, hydrocephalus, amaurosis, deafness, migraine, mania, epilepsy, scrofula, hydrothorax, asthma, dyspnea, ascites, chlorosis, hysteria, paralysis, scurvy, melancholia, leprosy, ulcers, and gout. It is of interest that young Humphrey Davy was brought from Penzance in Cornwall (where he had been working, as a doctor's assistant, on the physiological effects of nitrous oxide) to be a member of the staff of the new pneumatic institute. It is of further interest that in these early experiments of Davy, nitrous oxide was inhaled only in concentrations so dilute as to produce euphoria and excitement and that it was considered, at first, mainly for its possible therapeutic effects in various diseases.

In 1813, Courtois (*2570*), in a medical thesis presented to the Faculty in Paris, reviewed the physiological effects of air under pressure and predicted that it may have a therapeutic value.

The first pressure chamber constructed in the nineteenth century to investigate the physiological effects and therapeutic action of compression and rarefaction of the air on the human body was built by Junod and described by him in 1834 (*2574*). This chamber was a sphere of copper 1.4 m. in diameter equipped with a thermometer and barometer, and designed for the production of pressures greater or lower than 1 atmosphere. In general, moderate pressures only were investigated. At a pressure of 1½ atmospheres (absolute), Junod reported symptoms referable to the middle ear. Respiration was reported as being easier, deeper, and slower. Vital capacity was increased and there was a subjective feeling of agreeable warmth in the chest. The pulse was stated to be full and rapid. Junod

believed that the superficial vessels became constricted and that there was a greater circulation in internal organs such as the brain. This was believed to account for a supposedly enhanced mental activity in subjects under pressure. Digestive functions were stated to be improved and increased secretion of saliva and urine was reported. It was also claimed that muscle power was enhanced.

Junod also described rigid copper cylinders into which the limbs could be inserted and subjected to local pressure or suction. On compression of the limbs, there was pallor of the skin as well as general systematic effects; on decompression, there were, in addition to general effects, local reddening of the skin and increased temperature of the limb as well as an engorgement which persisted some time after the treatment. Junod cited cases of paraplegia in which the "hemospastic apparatus," as these tubes were called, apparently produced some beneficial results.

Junod's pneumatic chamber was not well received. This was partly because the chamber was small and the pressure changes rapid which led to troublesome symptoms. Magendie (see von Vivenot (*2593, 2594*) 1870), who was appointed to investigate Junod's researches as a referee, reported to a commission chosen by the Academy of Science that the pneumatic chamber showed no promise of therapeutic value.

Investigations similar to those of Junod were also carried out by Tabarié (*2588, 2637*) 1838 and 1840 who investigated the effects of atmospheric condensation and rarefaction, applied not only locally but also to the entire body. Tabarié stressed the importance of gradual changes in pressure and a longer stay at the raised pressure level. He proposed the use of the following procedures in the treatment of disease: (*a*) general condensation of air over the whole body in a pressure chamber, (*b*) condensation locally applied to the limbs, (*c*) rarefaction of the air locally applied to the limbs, (*d*) alternate local condensation and rarefaction of the limbs (in effect, a pulsating procedure), (*e*) rarefaction of the air over the whole body except the head, and (*f*) alternate condensation and rarefaction over the whole body except the mouth. This latter procedure provides artificial respiration and was proposed in the treatment of suffocation.

In 1838, Tabarié (*2588*) reported results of 49 cases of respiratory disease treated in the pressure chamber in which some cures were claimed as well as many instances of improvement. Two hundred subjects, after a 2-hour stay in the chamber, showed an average slowing of the pulse of 10 to 20 beats per minute in contrast to the increase of pulse rate reported by Junod (*2574*).

In 1837–38, Pravaz (*2581*) gave an account of the application of compressed air "baths" (as treatments in the pneumatic chamber were called) to the treatment of tuberculosis, capillary hemorrhages, and catarrhal deafness. The author expressed his surprise that Junod had limited his investigations in the pressure chamber to purely physiological observations up to that time. His own pressure chamber, which he established in his orthopedic clinic in Lyons, France, was large enough to contain two persons and the air could be compressed or rarefied at will. He subjected himself to a pressure of 1½ atmospheres (absolute) on a stormy day when he had a headache and a feeling of lassitude. After 20 minutes in the chamber, he found himself free of malaise and felt a renewed sense of vigor. Pravaz used the compressed air "bath" on various patients suffering from post-influenzal anorexia and also suggested its use in convalescence from cholera. Success was claimed for the treatment of hemoptysis (cause not specified) and also in cases of young adolescent girls with frequent debilitating menstrual periods. Indications for such therapy were based on the belief that subjection of the body to raised atmospheric pressure causes a redistribution of blood from the periphery to the more central organs of the body, a theory refuted nearly a century later by Hill (*1083*). Pravaz believed that compressed air "baths" tended to dilate the lung passages. He subjected sufferers from pulmonary tuberculosis in the early stages and individuals with phthisic family history to treatments in the pressure chamber, and claimed improvement in health. Thus began a long series of clinical trials of the use of the pressure

chamber in pulmonary tuberculosis and a protracted controversy as to the value of this procedure. The controversy has ended in a general agreement that raised atmospheric pressures are not of appreciable benefit in Koch's bacillus infections of the lungs. During the second half of the nineteenth century, however, this treatment continued to have vogue and institutes for pneumatotherapy, using the pressure chamber, were established in many European centers and even in the twentieth century the treatment has been continued sporadically.

Pravaz also used the pressure chamber in cases of catarrhal deafness and dysacousia on the assumption that raised air pressure reduces engorgement of mucosal surfaces. He also established indications for pressure therapy in acute and chronic catarrh, emphysema, pleuritic exudation, whooping cough, chlorosis, and scrofula. Like Tabarié, Pravaz also reported slowing of the pulse in patients exposed to raised pressures in the chamber and ascribed the acceleration reported by Junod to the small size of the latter's chamber in which the pressure fluctuated with each thrust of the pump.

Pravaz's work was approved and hailed as a new therapeutic method of promise by a commission chosen by the Academy of Medicine of Lyons. In 1853, the Paris academy awarded the Monthyon Prize jointly to Junod, Tabarié, and Pravaz in recognition of their work.

In 1840, Pravaz (*2583*) reported the construction of a chamber capable of receiving 12 patients at a time. He accepted patients suffering from anorexia, menorrhagia, and chronic affections of the larynx and trachea and stressed its value in scoliosis and other chest deformities as a method to be used in conjunction with remedial exercises in children. In treating debilitated patients suspected of pulmonary tuberculosis, Pravaz did not claim success in advanced cases but he did believe that the treatment often delayed the progress of the disease. Cases of pleurisy were held to be successfully treated (*2584*).

Junod also applied the method of the pneumatic chamber to the treatment of pulmonary tuberculosis and in 1842 (*2668*), described the case of a young girl of 13 with "incipient tuberculosis" who was given treatments in the chamber at 3 atmospheres (absolute) with the disappearance of symptoms of 3 years' standing. This report is of particular interest since the pressures used were somewhat more comparable to those encountered in underwater operations than were the pressure levels usually reached in the use of therapeutic pneumatic chambers.

A significant contribution to the field of the therapeutic use of pressure chambers was made by Bertin (*2640*) who published, in 1855, an extensive monograph outlining the history of the development of pneumatic chambers and described the physiological effects of compressed air "baths." He also outlined the indications for therapy in acute and chronic bronchitis, laryngitis, catarrh, emphysema, asthma, hemoptysis, irregular menstruation, whooping cough, and pulmonary tuberculosis.

In 1852, Milliet, see von Vivenot (*2593*, *2594*) 1870, founded another medical pneumatic establishment at Lyons and in 1854 constructed a chamber in Nice. Milliet's compression chambers were large enough to hold one, two, or more patients. He also built a large circular chamber, 10 ft. in diameter, which accommodated 10 to 12 subjects at one time. This chamber had a lock or vestibule through which entrance and egress could be effected without disturbing the course of the chamber run. The compression pumps were operated by two steam engines, 3- and 12-horsepower respectively. Patients were pressurized to 1½ to 1⅔ atmospheres (absolute). Runs lasted for 2 hours—½ hour for the rise to maximum, 1 hour at maximum pressure, and ½ hour for decompression. The importance of gradual change in pressure was stressed and the only disturbing sensation during compression was a slight blocking in the ears which could be cleared by swallowing or blowing the nose. Patients showed a lowering of pulse rate in the chamber and a reduction in respiratory rate. Milliet recommended, on the average, 30 to 40 treatments. The procedure was advised in catarrh, emphysema,

and in the early stages of pulmonary tuberculosis.

In his paper published in 1855, Milliet (*2607*) reported favorable results in cases of laryngitis, aphonia, chronic bronchitis, asthma, emphysema, anemia, whooping cough, catarrh, and pulmonary tuberculosis (diagnosis not determined). Although a critical appraisal of these cases as well as other clinical reports in the literature, both previously and subsequently, casts grave doubt as to any persistent clinical improvement in tuberculosis, it does seem that patients enjoyed some symptomatic relief and in cases of asthma, emphysema, and chronic bronchitis, this seems certainly to have been the case.

In 1860, Grindrod (*2665*) published a monograph describing a therapeutic pressure chamber in Malvern, England, one an antechamber and the other a large pressure chamber capable of containing 8 to 10 subjects. Relief was claimed in asthma, aphonia, catarrh, deafness, and early phthisis. This monograph provides a useful summary of the history of the treatment up to 1860. It also contains a description of Grindrod's chambers and programming of the runs. The physiological action of pressure was described and indications for therapy were given. Grindrod claimed that there was no enlargement of the thorax during the course of the pressure run but noticed freedom from oppressed breathing in cases of asthma, emphysema, and bronchitis in which patients suffered from labored breathing. Respirations tended to be less frequent in such cases and it was claimed that there was more efficient oxygenation of the blood.

In 1863, von Vivenot (*2591*) recommended the establishment of a therapeutic pressure chamber at Vienna and in 1867, Sandahl (*2701*), in a 60-page monograph, described the history of the Medical Pneumatic Institute in Stockholm. This monograph contains a review of published work on the therapeutic uses of compressed air chambers and indications for such therapy. Three reports of von Vivenot's (*2592, 2593, 2594*) appearing in 1868 and 1870 may be consulted for complete historical accounts of the subject. von Vivenot's 626-page monograph (*2592*) published in 1868, is particularly complete and contains a critical analysis of the early investigations on the therapeutic effects of high pressure, from Henshaw's work in the seventeenth century up until 1868. The construction of pressure chambers was also described, as well as the physiological effects of high pressure on the special senses, respiration, muscular contraction, metabolism, and circulation. Indications for therapy were given in great detail.

In 1861, a chamber was established by Josephson (*2667*) 1864 and mention should also be made of the investigations of Lange (*2670*) 1863 and Levinstein (*2680*) 1867. von Liebig (*2627*) 1888 called attention to chambers in use at Baden-Baden and other places. In his own institute at Reichenhall near Munich, there were 5 chambers capable of accommodating a total of 50 patients at one time. von Liebig's report is based on the treatment of 510 patients, and the physiological effects of the treatment as well as clinical indications are described. A description of the use of pressure chambers at Reichenhall was given by Burdon-Sanderson (*2647*) in 1868.

In 1885, Williams (*2595*) reviewed the therapeutic uses of pressure chambers and described the chamber in use at the Brompton Hospital for Consumption and Diseases of the Chest in London. This chamber was 8 ft. in diameter, 8 ft. high, and accommodated four patients. The compression pumps were operated by an 8-horsepower steam engine and compressed air was stored in a central reservoir to make the air supply even and steady. The maximum gauge pressure used was about 10 lb. per sq. in. or approximately two-thirds of an atmosphere above ambient pressure. Individual treatment lasted 2 hours and 12 to 100 sessions were given, according to the particular case. Claims were made for the method in cases of emphysema, chronic bronchitis, whooping cough, asthma, and chlorosis. It was stated that respiration was easier and that the diaphragm descended lower during each inspiration than at ambient pressure. The author also insisted that compression resulted in intropulsion of the blood from skin and mucosal surfaces to more deeply lying organs.

One of the most active clinics practicing pneumatic therapy was the Pneumotherapeutic Institute in Brussels. The history of this organization was described by Hovent (*2573*) in 1891. The clinic was founded in 1879 by a group of prominent Belgians, and Despalles, a Belgian neurologist and aerotherapist, was asked to organize and direct it. The institution provided chamber therapy at pressures above or below atmospheric pressure and also treated patients by inhalation of compressed air and exhalation into rarefied air. There were also provisions for the sale and distribution of oxygen for therapeutic uses. There were 7 pressure chambers capable of accommodating 2 to 10 persons each and these could be connected with tanks containing compressed air, rarefied air, nitrogen, or oxygen. Circulation and purification of air was provided for and vapors could be added as desired. It was claimed that the pulmonary alveoli were expanded by raised pressure and that the diaphragm descended lower with each inspiration. Respiration was slower and the pulse slower and fuller. Compressed air "baths" were recommended in asthma, emphysema, chronic bronchitis, and whooping cough. The use of compressed air "baths" in pulmonary tuberculosis was also considered. In the discussion of this paper, which was read before the Philadelphia County Medical Society in 1891, Wilson stated that many who had at first claimed excellent results from the pneumatic chamber had now abandoned its use. In the same discussion, Solis-Cohen pointed out that the inspiration of compressed air outside the chamber was no longer recommended in active tuberculosis and that tuberculosis had been long laid down as a contraindication for such therapy by Waldenburg and others, particularly in cases with lung cavities.

For further historical accounts of therapeutic uses of high pressure air, the reader may consult a large monograph by Simonoff (*2587*) published in 1876, which contains an excellent bibliography; a thesis by Grand (*2572*) published in 1877; Mullier's (*2578*) paper published in 1878; and a report by Pramberger (*2580*) 1879. A report by Dujardin-Beaumetz (*2571*) 1888 may be consulted by those desiring a concise review of the subject.

Particular attention should be directed to *De pneumatische therapie* published in Amsterdam by Arntzenius (*2559*) in 1887. This monograph is written in Dutch but it is particularly useful because of its bibliography of some 300 references on pneumatic therapy both with compression chambers and portable apparatus for respiration of composed or rarefied air. For modern commentaries on the clinical use of pressure chambers, reference may be made to Diener (*2616*) 1936, Beaumont (*2639*) 1937, and Blumauer (*2614*) 1940.

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B. DESCRIPTION OF THERAPEUTIC PRESSURE CHAMBERS AND PROGRAMMING OF TREATMENTS

The compression chamber constructed by Junod (*2574*) was a simple copper sphere 1.3 m. in diameter. It was equipped with a thermometer and a mercury barometer, and was designed for either compression or rarefaction of the atmosphere. The pressures employed did not exceed 1½ atmospheres (absolute) except in certain experiments in which patients were taken to 3 atmospheres (absolute). Provision was made for circulation of the air but only very brief periods of exposure were used. Because of the small size of the chamber and the nature of the pump, there was considerable fluctuation of pressure within the chamber at each pump stroke.

Pressure chambers were rapidly improved by the early workers and the length of stay in the chamber was lengthened. Payerne (*2608*) 1852 believed that 3 hours was the limit of stay for therapeutic effects. He believed that compression should not exceed 400 mm. Hg above 1 atmosphere. Milliet (*2607*) in 1855 described his compression chambers capable of holding 1, 2, or more persons and also a large chamber capable of accommodating 10

to 12 patients at one time. This chamber was a large circular room, 10 ft. in diameter with a lock or vestibule for entry and exit without disturbing the pressure within. The pumps were operated by 2 steam engines of 3- and 12-horsepower respectively. In the small chambers, a ventilation of air of 300 cu. ft. per hour was maintained while in the large chamber there was a circulation of 5,000 cu. ft. of air per hour. A pressure of $1\frac{1}{5}$ atmospheres (absolute) was regularly employed, the maximum pressure used being $1\frac{2}{3}$ atmospheres (absolute). Patients remained in the chamber for 2 hours, one-half hour being occupied in raising the pressure to maximum, 1 hour at maximum pressure, and one-half hour for decompression to normal pressure. Although subsequent workers have used various times of stay in the chamber, the schedule used by Milliet appears to have been the one most adhered to. The number of treatments required for a therapeutic effect was stated by Milliet to be variable and dependent upon the condition to be treated. However, the average number of compressed air "baths" required was believed to be 30 to 40. Improvement in asthma was reported by Milliet after the tenth session in the chamber and in a case of emphysema, complete recovery was claimed after 50 treatments. In a case of asthma in a young woman of 29 years of age, symptoms disappeared after 100 treatments. In cases of chronic catarrh, 30 treatments appeared to suffice and in a female child of 5 years of age, chronic cough and vomiting in pertussis were abolished after 17 sessions in the chamber.

The reader should consult Simpson's monograph (*2609*) 1857 which contains a description of a cylindrical iron pressure chamber for therapeutic use in Otley, Yorkshire. This chamber was pressurized by pumps operated by steam engines. Simpson recommended the use of the chamber in phthisis as well as asthma, chronic bronchitis, and emphysema. The report contains a description of 20 of the author's cases as well as cases reported by other early workers.

One of Grindrod's chambers (*2665*) 1860 was a steel cylinder 14 or 15 ft. high and 10 ft. in diameter and accommodated 10 to 12 patients. Air was constantly circulated through the chamber, a pressure of $1\frac{1}{2}$ atmospheres (absolute) being maintained. The temperature of the interior of the chamber was regulated and treatments lasted 2 hours, the sessions following the program recommended by Milliet, namely, one-half hour to maximum pressure, 1 hour at maximum pressure, and one-half hour for decompression. As to the number of treatments, Grindrod believed that probably no less than 20 sessions would be of value. Sometimes, after about 12 to 15 treatments, there was a recrudescence of the original symptoms for 2 or 3 days but these finally yielded on continuation of treatment.

Another description of an early therapeutic pressure chamber was given by Fischer (*2600*) 1864–65. This chamber operated at $1\frac{2}{5}$ atmospheres (absolute) and was of cylindrical construction, being 8 ft. high and 6 ft. in diameter. In a report published in 1865, von Vivenot (*2610*) recommended daily $1\frac{1}{2}$-hour sessions at pressures of $1\frac{3}{7}$ atmospheres (absolute) for a permanent increase in vital capacity.

Lee (*2605*) in 1867 called attention to pneumatic chambers set up for therapeutic use in Toronto, Canada, and Rochester, N.Y. It appears that such therapy was little known in the United States at that time and what chambers did exist were in the hands of "laymen or empirics." Lee described a pressure chamber then being set up in Buffalo with an air flow of 50 to 100 cu. ft. per minute and capable of creating pressures of $1\frac{1}{2}$ to 4 atmospheres (absolute) or even higher. Sessions lasted for 2 hours according to the Milliet schedule and the treatment was believed to be indicated in cases of rheumatism, neuralgia, hypochondriasis, asthma, chronic bronchitis, amenorrhea, and incipient tuberculosis.

Lange (see Bricheteau (*2599*) 1868) operated his chamber at $1\frac{1}{2}$ atmospheres (absolute) going to maximum pressure in 20 to 25 minutes, remaining at maximum for 1 hour and decompressing in 30 to 40 minutes. Requirements in the uses of the technique were described by Lange in 1870 (*2603*). It was claimed that in the chamber respiration

became easier. The respiratory volume increased, the respiratory rate diminished, and the pulse rate decreased. Indications for treatment were: bronchitis, conjunctivitis, emphysema, asthma, pulmonary tuberculosis, and ear disturbances.

Another American description of therapeutic uses of compressed air chambers was that of Etheridge (*2617*) published in 1873. The chamber described was 8 or 9 ft. high and 6 ft. in diameter. In the center of the floor, there was an air-supply tube from a pump, while above this, there was a circular plate some 6 ft. in diameter with chairs for patients. Air exit was at the top of the chamber and the pressure within the chamber was controlled by a stopcock at the exit tube. Each treatment lasted 2 hours, following the Milliet schedule.

In describing the pneumatic chamber at Reichenhall, Goeschen (*2602*) in 1873 stated that patients were subjected to a pressure of 320 mm. Hg above 1 atmosphere for 2 hours. Pneumatic chambers typical of those in use in the second half of the nineteenth century were illustrated by Bogoslovsky (*2596*) 1876.

For a description of the chambers in use at Haarlem, reference may be made to a report by Fyan (*2601*) 1883. This author claimed that the use of the compressed air chamber resulted in an increase of vital capacity through its effect in lowering the diaphragm. An increased oxygenation of the blood was also reported. Thirty to sixty sessions were stated to effect improvement in chronic bronchitis, whooping cough, catarrh, and emphysema. Cases of anemia and chlorosis received 20 to 40 treatments, while in phthisis, 60 to 100 or more treatments were advised. To begin with, a pressure of $1\frac{1}{5}$ atmospheres (absolute) was used, increasing to $1\frac{1}{2}$ atmospheres as the patient became accustomed to the treatment.

The pneumatic installation at the Berlin Jewish Hospital, described by Lazarus (*2604*) in 1884, consisted of two chambers with a common lock between them. Patients were pressurized to 2 atmospheres (absolute), a sufficient air-flow being maintained to keep the concentration of carbon dioxide from rising to dangerous levels.

Bonte (*2598*) in 1903 published illustrations of pneumatic chambers at Reichenhall. At that date there were 11 chambers at Reichenhall with places for 86 patients. Sessions lasted $1\frac{3}{4}$ hours, 30 minutes being taken for rise to maximum pressure, 45 minutes at maximum pressure, and 30 minutes for decompression. Pressures of 200 to 360 mm. Hg above 1 atmosphere were used.

A modern description of a pneumatic chamber for therapeutic use was given by Diener (*2616*) 1936. This chamber operated at a pressure of $1\frac{1}{2}$ atmospheres (absolute) and treatments lasted $1\frac{3}{4}$ hours. It was claimed that respiratory rate was dimished, respiratory depth increased, and that the vital capacity was increased. Attention was called to the X-ray finding of a greater descent of the diaphragm during respiration in the chamber than before treatment. Blood pressure was hardly affected and there was little change in pulse rate. There was no essential alteration in gaseous exchange.

Blumauer (*2614*) in 1940 described a large pressure chamber at Bad Bleichenberg constructed of 15 mm.-thick steel plates with unshatterable glass windows. In the course of a run, the pressure was elevated slowly to 1.4 atmospheres (absolute), maintained for 45 minutes and returned to normal in 30 minutes. The temperature was kept at 20° C. and patients were subjected to approximately 20 to 30 sessions on successive days. It was claimed that the treatment produced a dilatation of the bronchi and bronchioles, thus relieving the intense dyspnea of asthma. Bronchial secretions were stated to be loosened and more easily coughed out. The diaphragm was stated to descend lower than normal, leading to greater expansion of the lungs. Gaseous exchange was believed to be facilitated. Blood pressure was little affected although sometimes there was a fall in pressure. It was stated that the pulse was slowed. The treatment was believed to be indicated in asthma and emphysema as well as bronchiectasis. It was stated to be contraindicated in pyrexial diasese, hypertension, and circulatory failure.

This report is of interest because it is relatively recent. However, no experiments are reported nor are results of controlled clinical observations given.

Attention should be called to a mobile pressure chamber for therapeutic use described by Fontaine (*2716*) 1879. This chamber was mounted on wheels. The interior was painted white and light was provided from 10 ports. The chamber was 2 m. wide by 3.5 m. long and 2.65 m. high. It was claimed that the interior would accommodate 10 to 12 people. The pressure within the chamber could be regulated from within or from the outside. Outside the chamber there was provided a small platform on which was mounted a pump capable of delivering 400 to 600 liters of air per minute. There was also an air-cooling device which maintained the temperature within one or two degrees of the ambient air temperature. The chamber was used for the pressure treatment of asthma, emphysema, chronic bronchitis, anemia, etc. Its principal use, however, was as a surgical operating room. Fontaine recommended the reduction of hernias in compressed air and the chamber was also used in the administration of nitrous oxide at pressures of 1¼ to 1⅓ atmospheres (absolute). The rationale of this procedure is described on page 321. A tank containing a mixture of nitrous oxide and oxygen under a pressure of 10 atmospheres was provided outside the chamber and this tank communicated with a bellows-like sac under the operating table within the chamber. The gas mixture was conveyed from the bellows reservoir to the patient on the operating table through a tube and rubber face mask. Air circulation was maintained within the chamber to prevent untoward effects on personnel attending the patient.

So much hope was held out for the use of compressed air chambers in surgery that Fontaine (*2716*) worked on the idea of a pressurized surgical amphitheater with a capacity of 300 persons! This was to be large enough to permit students and others to watch operations under increased pressure. There were to be provisions for heating and ventilation and locks to permit exit and entry of patients and other personnel without interfering with the pressure in the amphitheater. Fontaine reminded surgeons employing Lister's new antiseptic methods that phenol vapor could be introduced into his mobile pressure operating chamber, either before or during operation, via the air supply pump.

2596. Bogoslovsky, V. S. [*Air as a curative agent.*] Moskva, A. Torletsky and M. Terekhov, 1876, 24 pp.

2597. Bogoslovsky, V. S. [*Pneumatic clinic of V. S. Bogoslovsky.*] Moskva, A. Torletsky and M. Terekhov, 1876, 8 pp.

2598. Bonte, G. Pneumatische Kabinette und deren maschinelle Einrichtung. *Gesundheitsing.*, 1903, *26:* 365–368. [R]

2599. Bricheteau, F. Des effets physiologiques de l'air comprimé et de ses applications à la thérapeutique. *Bull. gén. Thér., Paris*, 1868, *75:* 203–208. [P, R]

2600. Fischer, G, Der Luftcompressionsapparat. *KorrespBl. Ärz. Apothek. Oldenb.*, 1864–65, *3:* 69–73; 81–85. [R]

2601. Fyan, S. Verslag der behandelde gevallen in de pneumatische inrichting te Haarlem. *Ned. Tijdschr. Geneesk.*, 1883, Tweede Reeks, *19:* 437–440. [R]

2602. Goeschen, A. Die pneumatische Kammer in Reichenhall. *Göschens Dtsch. Klin.*, 1873, *25:* 1–3. [P]

2603. Lange, [ ]. Einige Bemerkungen über die richtige Anwendung der verdichteten Luft. *Berl. klin. Wschr.*, 1870, *7:* 94–98. [C]

2604. Lazarus, [ ]. Das pneumatische Kabinet des jüdischen Krankenhauses zu Berlin. *Gesundheitsing.*, 1884, *7:* 40–43. [R]

2605. Lee, C. A. Extract from a lecture on the physiological and remedial effects of increased pressure of the atmosphere. *Buffalo med. J.*, 1867, *6:* 199–211. [R]

2606. Liebig, G. von Die pneumatischen Kammern und die Indicationen für den Gebrauch des erhöhten Luftdruckes. *Münch. med. Wschr.*, 1888, *35:* 285–287; 304–305. [R]

2607. Milliet, Joannis. *Compressed air as a remedial agent.* Nice, Société typographique, 1855, 83 pp. [C]

2608. Payerne, [ ]. Influence de l'air comprimé sur l'homme, sous quelques points de vue inétudiés. *Mém. Soc. Sci. nat., Cherbourg*, 1852, *1:* 145–151. [R]

2609. Simpson, Archibald. *Compressed air, as a therapeutic agent, in the treatment of consumption, asthma, chronic bronchitis, and other diseases.* Edinburgh, Sutherland and Knox, 1857, 40 pp. [R]

2610. Vivenot, R. von, Jr. Ueber die Zunahme der Lungencapacität bei therapeutischer Anwendung der verdichteten Luft. *Virchows Arch.*, 1865, *33:* 126–144. [P]

2611. Anon. Rasmussens medicopneumatiske Anstalt. *Hospitalstidende*, 1864, *7:* 137–138.

C. PHYSIOLOGICAL ACTION OF COMPRESSED AIR "BATHS"

The physiological responses of the body to high altitudes or the rarefied atmospheres of the decompression chamber may be profound. (See Hoff and Fulton (*3*) 1942 (references no. 213 to 2627) and Hoff, Hoff, and Fulton (*4*) 1944 (references no. 5813 to 6501). In contrast, the body is only slightly affected by compression up to 3 atmospheres (absolute) if pressure effects on the ears, changes in the tone of the voice, and certain psychic effects are excluded. Within these limits of pressure, it appears that the compression of the air does not lead to drastic readjustment of bodily economy and that it is well supported by the human organism. With compression to higher levels, the toxic action of oxygen and other narcotic effects begin to be severely limiting factors in bodily function. The literature bearing on the physiological effects of high pressures such as may be encountered in diving and caisson and tunneling operations is discussed on page 23. Although the reader will consult that literature for the major reports on bodily readjustments in compressed air, it may be worthwhile here to review and comment on the evidence concerning bodily changes in patients and healthy individuals subjected to the more moderate pressures of the therapeutic pneumatic chambers. This review will serve to point out certain basic fallacies upon which the theory of the therapeutic action of compressed air was based. However, in spite of the weakness and uncritical nature of much of the evidence, the literature here presented has played a definite role in the advancement of our knowledge of the responses of the organism to elevated pressures.

In 1835, Junod (*2575*, *2576*) observed the responses of human subjects to a pressure of 1½ atmospheres (absolute). There were painful symptoms referable to the middle ear which were clearly understood to be due to delay or failure in equalization of pressure between the middle ear and the exterior. These symptoms in most individuals disappeared on yawning or performing other maneuvers which opened the Eustachian tube. Respiration was stated to be slower, deeper, and easier and a sense of agreeable warmth in the chest was reported. With reference to the cardiovascular system, Junod found a tendency toward acceleration of the pulse and he claimed that there was a diminution in the caliber of superficial vessels. Circulation in more deeply situated organs, particularly the brain, was believed to be increased and this was held to be the explanation of the enhanced mental activity said to be characteristic at 1½ atmospheres. The functions of the gastrointestinal tract were believed to be increased and there was supposed to be a rise in urinary output. A characteristic finding was a subjective sense of well-being, increased muscular power, and sense of decrease of body weight. Pravaz (*2581*) 1937–38 also observed this freedom from lassitude and sense of enhanced motor power. It was Pravaz's opinion also that compression exerted a favorable influence on digestion and bodily secretions and he reported, as well, a peripheral vasoconstriction.

Tabarié (*2637*) 1840 and Pravaz (*2634*) 1849–50 both reported reduction in pulse rate. It is of interest that Heller, Mager, and von Schrötter (*28*) in 1900 reported an average diminution of 14.6 beats per minute in 35 men exposed to pressures of 3.5 atmospheres (absolute). There was no relation between the amount of slowing of the pulse and the height of the pressure to which subjects were exposed, a rise in pressure of less than ½ atmosphere producing as much change as an elevation of 2½ atmospheres. A slowing of the pulse was also reported by Hervier (*2620*) in 1849 who also called attention to increased appetite, increased motor power, and expansion of the thorax. Hervier found an initial rise in carbon dioxide output followed by a diminution. Poyser (*2633*) 1853 believed that compressed air "baths" permitted increased oxygenation of the blood and that this was responsible for the fall in pulse rate and the slower respiration. A mechanical effect was also claimed, arising from the supposed action of increased pressures in driving the blood to the internal organs from the periphery. For this reason, raised pressures were recommended in the relief of conjunctivitis, inflam-

matory conditions of the lungs, and in bronchitis.

Milliet (*2607*) 1855 also called attention to slowing of the pulse especially in patients suffering from asthma, emphysema, chronic bronchitis, or pulmonary tuberculosis. He stated that in such patients the pulse rate was diminished by 10, 15, or even 45 beats per minute and that there was a corresponding reduction in respiratory rate and an increase in body secretions. Similar findings were reported in 1853 by Calloch (*2615*), The reader is also referred to Bertin's lengthy monograph published in 1855 (*2640*) in which the views then current as to the physiological effects of pressurization in therapeutic chambers have been set forth. In describing physiological effects of pressurization in the pneumatic chamber, Haughton (*2619*) in 1858 found no essential change in pulse rate in pressures up to 2 atmospheres (absolute).

The physiological findings of von Vivenot (*2638*) 1860, Sandahl (*2635*, *2701*) 1865 and 1867, and Etheridge (*2617*) 1873 were all in essential agreement with those of Junod, Tabarié, and Pravaz. Etheridge referred to a statement by Junod that under the influence of raised pressures, there is a flow of rich ideas with a tendency of "verse making"! The findings of von Liebig (*2625*) 1874 also coincided with those of the other observers. The effects of raised pressure were also set forth in a thesis published by Grand (*2572*) in 1877. Forlanini (*2618*) 1877 and Mosso (*2630*) 1877-78 reiterated the view, which recurs constantly in the literature, that the superficial circulation is diminished.

Some attention was given by early workers to the effects of raised pressure in the pneumatic chamber on the form of the pulse curve. (See Knauer (*2622*) 1878.) von Liebig (*2626*) 1884 reported changes in the pulse curve but Hill (*1083*) 1912 found no significant change in the form of the curve in compressed air. Lazarus (*2624*) 1882 reported constriction of the skin capillaries of dogs in compressed air chambers and believed also there was an elevation of blood pressure. He doubted whether the diaphragm was depressed from compression of gases in the intestines but upon this point experimental results were doubtful. Lazarus stated that raised atmospheric pressures tended to dilate obstructed bronchi and helped to free them of mucous plugs.

Suchorsky (*2636*) 1884 reported a reduction in the amount of expired carbon dioxide and a fall in the respiratory quotient. The rate and volume of respiration were reduced, particularly in patients with chronic pulmonary diseases who were subjected to raised pressure. The effects of raised pressure on pulse and respiration were reviewed by von Liebig (*2627*) 1888.

It is quite clear that in healthy subjects there may be little or no change in pulse rate, whereas in patients with rapid pulse associated with dyspnea there may be a really marked slowing. In an attendant who worked in von Liebig's chamber for 4 years, the normal respiratory rate in free air fell from 12 to 16 per minute down to 4 or 5.

Some degree of vasoconstriction of skin and in mucous membranes and slowing of pulse were reported by Hovent (*2621*) 1891. Phillips (*2632*) 1902 called attention to pallor of skin and mucosal surfaces as well as reduction in respiratory rate, increase in vital capacity, and slowing of the heart. Improved oxygenation was noted by Bonte (*2598*) 1903 as well as by Hoffenreich (*2666*) 1904.

Nelson (*2631*) 1928 believed that compressed air exerted a physiological effect comparable to oxygen-enriched air at normal pressures and acted to relieve air hunger due to obstructing lung exudates. Relief was also claimed in localized edema and chronic indolent ulcers. In Diener's report published in 1936 (*2616*) it was again stated that the respiratory rate is reduced in patients in the pneumatic chamber and that there is an increase in total thoracic capacity. Little change was found in the blood pressure and there was but slight change in the pulse rate and no essential alteration in total gaseous exchange.

Blumauer (*2614*) 1940 called attention to increased descent of the diaphragm in the pressure chamber as well as to dilatation of bronchioles and consequent loosening of

bronchial secretions. Blumauer stated that the blood pressure was little affected, there being usually a slight fall; the pulse was usually slowed. Regarding the lowering of the diaphragm or a change in vital capacity, Heller Mager, and von Schrötter (*28*) 1900 found no definite evidence on these points by percussion. As Hill (*1083*) 1912 has stated, quantity of abdominal gas varies considerably from one individual to another so that the compression effect, while negligible in some, may be considerable in others. It has been frequently reported that many caisson workers observe a diminution in abdominal girth while exposed to high pressures.

2612. Aron, E. Ueber Hämoglobin-Bestimmungen und die Sauerstoff-Kapaztät des Blutes bei Aenderung des Atmosphärendruckes im pneumatischen Kabinette. *Z. klin. Med.*, 1912, *75:* 126–135. [P]

2613.* Benczúr, G. and Z. Rausch. Die Wirkung des erhöhten Luftdruckes der pneumatischen Kammer auf die Blutzirkulation. *Z. ges. phys. Ther.*, 1932, *42:* 207–211.

2614. Blumauer, F. Die Behandlung in der pneumatischen Kammer. *Wien. med. Wschr.*, 1940, *90:* 367–369. [M]

2615. Calloch, F.-M.-Constant. *De la pression atmosphérique, considérée au point de vue médical.* Thèse (Méd.) Paris, Rignoux, Imprimeur de la faculté de médecine, 1853, 46 pp. [C, R]

2616. Diener, I. Über die Anwendung "pneumatotherapeutischer Verfahren" im Kurort. *Med. Welt*, 1936, *10:* 616–618. [P, R]

2617. Etheridge, J. H. Compressed air. *Chicago med. J.*, 1873, *30:* 166–171. [R]

2618. Forlanini, C. Della azione meccanica del bagno d'aria compressa. *Gazz. med. lombarda*, 1877, Ser. 7, *37:* 121. [P]

2619. Haughton, E. On the use of the compressed air-bath. *Dublin Hosp. Gaz.*, 1858, *5:* 56–57. [R]

2620. Hervier, P. Note sur la carbonométrie pulmonaire dans l'air comprimé. *Gaz. méd. Lyon*, 1849, *1:* 168–169.

2621. Hovent, [ ]. The pneumo-therapeutic institute of Brussels. *Cincinn. Lancet-Clin.*, 1891, N. ser., *26:* 795–798. [R]

2622. Knauer, Heinrich. *Ueber den Einfluss des Aufenthalts in verdünnter Luft auf die Form der Pulscurve.* Inaug.-Diss. (Med.) Berlin, Gustav Schade, 1878, 32 pp. [R]

2623. Lange, [ ]. Ueber die Wirkungen der comprimirten Luft auf den Organismus. *Jber. Ges. Naturk. Dresden*, 1865–66 (3. März): 33–37. [P, R]

2624. Lazarus, [ ]. Ueber pneumatische Therapie. *Dtsch. med. Wschr.*, 1882, *8:* 681–682. [P, R]

2625. Liebig, [ ]. von. Der Gasaustausch in den Lungen unter dem erhöhten Luftdrucke der pneumatischen Kammer. *Ärzt. IntelligBl.*, 1874, *21:* 151–154. [P]

2626. Liebig, G. von. Die Veränderung der Pulscurven in der pneumatischen Kammer. *Dtsch. med. Wschr.*, 1884, *10:* 289–291. [P]

2627. Liebig, G. von. Die Anwendung der pneumatischen Kammern bei Herzleiden. *Dtsch. med. Wschr.*, 1888, *14:* 1066–1068. [P]

2628. McCrudden, F. H. Insufficient oxygen supply as a factor in disease. *Boston med. surg. J.*, 1916, *175:* 480–483.

2629. Milliet, J. De l'air comprimé au point de vue physiologique. *Gaz. méd. Lyon*, 1856, *8:* 172–177; 197–203. [P, R]

2630. Mosso, A. Sull'azione fisiologica dell'aira compressa. Esperienze ed osservazioni. *Arch. Sci. med.*, 1877–78, *2:* 147–176. [P]

2631. Nelson, C. F. The use of compressed air as a therapeutic agent. *J. Kans. med. Soc.*, 1928, *29:* 370–374.

2632. Phillips, C. D. F. The physiological actions and therapeutical uses of oxygen, ozone and compressed air. *Med. Brief*, 1902, *30:* 193–202. [P]

2633. Poyser, T. On the treatment of chronic and other diseases by baths of compressed air. *Ass. med. J.*, 1853: 797–799. [R]

2634. Pravaz, [ ]. Note sur la pression atmosphérique dans ses rapports avec le mécanisme de la respiration, le phénomène de l'hématose et la circulation capillaire. *Bull. Acad. Méd. Paris*, 1849–50, *15:* 520–532. [C, P, R]

2635. Sandahl, O. T. Nyare undersökningar och iakttagelser rörande de fysiologiska och terapeutiska verkningarne af bad i förtätad luft. *Hygiea, Stockh.*, 1865, *27:* 337–353. [R]

2636. Suchorsky, N. Zur Lehre von der Wirkung verdichteter Luft auf die Respiration. *Zbl. med. Wiss.*, 1884, *22:* 433–435. [P]

2637. Tabarié, [ ]. Sur l'action therapeutique de l'air comprimé. *C. R. Acad. Sci., Paris*, 1840, *11:* 26–28. [P, R]

2638. Vivenot, R. von. Ueber den Einfluss des veränderten Luftdruckes auf den menschlichen Organismus. *Virchows Arch.*, 1860, *19:* 492–522. [P, R]

D. INDICATIONS FOR AND CLINICAL EVALUATION OF COMPRESSED AIR "BATH" THERAPY

The first case treated by Pravaz (2581) 1837-38 in his newly constructed therapeutic pressure chamber was a young girl afflicted with a lateral deviation of the spine. This patient was greatly debilitated and was bed-

ridden every winter. She was given gymnastic exercises and sessions in the compressed air chamber. Pravaz reported great improvement in her health and in the influenza epidemic in 1837, she alone, of all her friends, escaped the disease. Pravaz made use of compressed air "baths" in treating many cases of post-influenzal depression and anorexia following this epidemic. Pravaz also used compressed air "baths" in various nutritional disturbances and in chronic affections of the larynx and trachea. He also made use of the newly devised treatment in malnourished children afflicted with chest deformities associated with pulmonary diseases. In all of these cases, it was claimed that the treatment led to expansion of the chest, reduction of the deformity, relief of dyspnea and other symptoms, as well as gain in weight, improvement in nutrition, and restoration of strength. Several young people with tubercular family history presenting such signs and symptoms as cough, dyspnea, hemoptysis, hectic fever, and lassitude were reported improved by repeated treatments in the pressure chamber. Pravaz did not claim that compressed air cured all cases of pulmonary tuberculosis, but he did believe that the therapeutic method had prophylactic value, especially in children, and that it would often arrest the disease. In almost every case, there was apparently symptomatic relief which made the treatment very acceptable and desirable to patients.

Pravaz also turned his attention to cases of catarrhal deafness. He claimed that the method acted partly by reducing engorgement of the pharyngeal mucosa. Some success was also claimed in cases of chronic laryngitis, and Pravaz also reported favorable results in a patient with acute conjunctivitis. Since raised atmospheric pressure was supposed to reduce congestion of various skin and mucosal surfaces, Pravaz also applied his newly devised method to cases of menstrual disorder and claimed that compressed air treatments corrected the immoderate flow of the menses in menorrhagia.

Compression chamber therapy found its chief application in the management of respiratory diseases and, although the quality of the evidence available makes it difficult to formulate an accurate clinical evaluation of the results of the treatment, it does seem that if high pressures have any curative value whatever, it is principally in such conditions as chronic bronchitis, emphysema, and asthma that the method may have had beneficial effects. In cases of acute laryngitis, some with loss of voice, compressed air "baths" were recommended by Milliet (*2607*) 1855, Sandahl (*2699*, *2700*, *2702*) 1865 and 1869, and Gent (*2662*) 1869. In chronic laryngitis, favorable reports of treatment were given by Pravaz (*2584*) 1840, Bertin (*2640*) 1855, Storch (*2705*) 1865, Sandahl (*2699*) 1865, Bordier (*2643*) 1877, and Moeller (*2691*) 1881. Moeller's paper may be consulted for case histories.

For a consideration of the use of compressed air in "croup," the reader should consult Caffe (*2648*, *2649*) 1863. References to compressed air therapy in whooping cough may be found in the papers of Milliet (*2607*) 1855, Bertin (*2640*) 1855, Lange (*2670*) 1863, Sandahl (*2701*) 1867, von Liebig (*2681*, *2685*) 1872 and 1883, Féréol (*2656*) 1873, Bordier (*2643*) 1877, Charrier (*2651*) 1880, Lessdorf (*2678*) 1881, Moeller (*2692*) 1881, Fyan (*2661*) 1882, and Hovent (*2621*) 1891.

With regard to the treatment of pertussis in the pressure chamber—a method which appears to have had some success—it may be recalled that more recent literature indicates that rarefied atmospheres in decompression chambers or at high altitudes may play a beneficial role in abolishing the cough and vomiting which are so difficult to eradicate in whooping cough. These papers are cited by Hoff and Fulton (*3*) 1942 as follows: Broekema (No. *4921*), Chaminaud (No. *4925*), Clamann and Becker-Freyseng (No. *4927*), Delgado Correa (No. *4933*), Kettner (No. *4962*), Nagel (No. *4986*), Pedemonte (No. *4991*), and Pflug and Jungheim (No. *4992*). Hoff, Hoff, and Fulton (*4*) 1944 add the following references: Kujath (No. *7483*), Morhardt (No. *7485*), Schütte (No. *7487*), and an unsigned article in the British Medical Journal in 1942 (No. *7490*).

In acute bronchitis, only three references to beneficial effects of compressed air therapy

have been found: Bertin (*2640*) 1855 and Sandahl (*2699*, *2702*) 1865 and 1869. In chronic bronchitis, however, extravagant claims have been made in the literature. Reference may be made to papers by Milliet (*2607*) 1855, Bertin (*2640*) 1855, Storch (*2705*) 1865, Sandahl (*2699*, *2702*) 1865 and 1869, Weber (*2710*) 1866, Lee (*2605*) 1867, Werber (*2711*) 1867, Gent (*2662*) 1869, Bordier (*2643*) 1877, De Cock (*2654*) 1878, Moeller (*2691*, *2692*) 1881, Fyan (*2661*) 1882, and Hovent (*2621*) 1891.

Even greater claims for therapeutic value of compressed air "baths" were made in the treatment of emphysema, most investigators asserting that repeated treatments reduced dyspnea and resulted in slower, easier respirations and greater elasticity of the lungs. The following papers may be consulted for a discussion of the use of compressed air chambers in emphysema: Milliet (*2607*) 1855, Bertin (*2640*, *2641*) 1855 and 1861, Grindrod (*2665*) 1860, Lange (*2670*, *2672*) 1863 and 1874, Levinstein (*2679*, *2680*) 1864 and 1867, Storch (*2705*) 1865, Sandahl (*2700*, *2701*) 1865 and 1867, Freud (*2658*, *2659*) 1865 and 1866, Brodowskiego (*2645*) 1866, Weber (*2710*) 1866, Werber (*2711*) 1867, Glas (*2663*) 1867–68, Lehmann (*2676*) 1876, Bordier (*2643*) 1877, De Cock (*2654*) 1878, Lessdorf (*2678*) 1881, Moeller (*2691*) 1881, Fyan (*2661*) 1882, Arntzenius (*2559*) 1887, Hovent (*2621*) 1891, Blumauer (*2614*) 1940, and Beaumont (*2639*) 1937.

The paper of Arntzenius (*2559*) 1887 may be consulted for detailed case histories of the use of pressure chambers in emphysema. Beaumont's paper contains a report of nine cases of moderately severe emphysema given treatment in the compressed air chamber. All but one showed improvement but in no case was there any increase in vital capacity during or after the compressed air "baths."

According to Lazarus (*2675*) 1883, the pressure chamber finds its main indication in bronchial catarrh and favorable results were reported by a large number of early workers. Since it is now known that raised atmospheric pressures do not produce an appreciable alteration in the circulation in mucous membranes, it is difficult to formulate any physiological basis upon which such a treatment might rest. Readers wishing to familiarize themselves with the evidence that exists in the literature should consult the following references: Milliet (*2607*) 1855, Bertin (*2640*) 1855, Caffe (*2649*) 1863, Levinstein (*2679*) 1864, Sandahl (*2699*, *2701*) 1865 and 1867, Freud (*2658*, *2659*, *2660*) 1865, 1866, and 1870, Werber (*2711*) 1867, Glas (*2663*) 1867-68, Pundschu (*2695*) 1868, Runge (*2698*) 1868, Gent (*2662*) 1869, Marc (*2689*) 1871, von Liebig (*2681*, *2682*, *2683*, *2684*, *2685*) 1872, 1875, 1877, 1879, and 1883, Lange (*2673*, *2674*) 1876 and 1877, Lehmann (*2676*) 1876, Fyan (*2661*) 1882, Lazarus (*2675*) 1883, and Arntzenius (*2559*) 1887.

The clinical evidence in the literature on the treatment of asthma in the compressed air chamber is not well controlled. However, there is such a large body of evidence as to constitute a definite indication that such therapy probably was of some value, at any rate in relieving symptoms. Specific reference is made to pressure chamber treatment of asthma by the following workers: Milliet (*2607*) 1855, Bertin (*2640*, *2641*) 1855 and 1861, Grindrod (*2665*) 1860, Caffe (*2648*, *2649*) 1863, Lange (*2670*) 1863, Levinstein (*2679*, *2680*) 1864 and 1867, Storch (*2705*) 1865, Sandahl (*2699*, *2700*) 1865, Freud (*2659*) 1866, Lee (*2605*) 1867, Werber (*2711*) 1867, Pundschu (*2695*) 1868, Gent (*2662*) 1869, Marc (*2689*) 1871, von Liebig (*2681*) 1872, Canuet (*2650*) 1873, Féréol (*2656*) 1873, Lehmann (*2676*) 1876, Bordier (*2643*) 1877, Lange (*2674*) 1877, Lessdorf (*2678*) 1881, Moeller (*2691*, *2692*) 1881, Arntzenius (*2559*) 1887, Hovent (*2621*) 1891, Hoffenreich (*2666*) 1894, and Blumauer (2614) 1940.

Although many early workers were impressed with the beneficial effects of pressure chamber treatment in patients suffering from pulmonary tuberculosis, this method of treatment has gradually fallen out of use. Pravaz (*2581*) 1837–38 and Bertin (*2640*) 1855 both recommended compression chamber treatment for hemoptysis and Pravaz (*2583*, *2584*) 1840 considered that the procedure arrested cases of "threatened" pulmonary tuberculosis. Sandahl's findings (*2701*) in 1867 were

not so optimistic. In almost all reports of pressure therapy in pulmonary tuberculosis, an accurate evaluation of the efficacy of the treatment is difficult or even impossible in the absence of accurate radiological and bacteriological diagnosis and, although in many cases symptomatic improvement was reported, X-ray and laboratory studies were lacking to confirm actual improvement. The question of pressure therapy in tuberculosis is in somewhat the same state at present as is the treatment of tuberculosis at high altitudes. Very probably, neither compression nor rarefaction of the atmosphere have any specific action on the progress of the disease. Those desiring to explore the literature in this field in greater detail should consult: Pravaz (*2583*, *2584*) 1840, Junod (*2668*) 1842, Devay (*2655*) 1853–54, Milliet (*2607*) 1855, Bertin (*2640*) 1855, Grindrod (*2665*), 1860, Lange (*2670*) 1863, Levinstein (*2679*) 1864, Storch (*2705*) 1865, Sandahl (*2699*, *2700*, *2702*) 1865 and 1869, Freud (*2658*, *2659*) 1865 and 1866, Fordier (*2643*) 1877, De Cock (*2654*) 1878, Moeller (*2691*, *2692*) 1881, Fyan (*2661*) 1882, and Arntzenius (*2559*) 1887.

Regarding therapy of other respiratory diseases, there remains to be mentioned reports by Sandahl (*2699*, *2700*) 1865 recommending the pressure chamber in bronchiestasis. Papers on the pneumatic treatment of atelectasis by Werber (*2711*) 1867 and Hoffenreich (*2666*) 1904 may also be consulted. Although Pravaz (*2581*, *2582*, *2583*, *2584*, *2585*) 1837–38, 1840, and 1841 recommended pressure chamber therapy in deformities of the chest and spinal curvature due to unilateral pulmonary diseases and although such treatment was also described by Debout (*2653*) 1851, Bertin (*2642*) 1866, and Bordier (*2643*) 1877, this form of therapy has completely dropped out of use.

Indications for compressed air chamber therapy in diseases of the blood and circulation were based upon the view that raised atmospheric pressure causes an intropulsion of blood to the internal organs and on the fact that compressed atmospheres supply oxygen to the body at a raised tension. Favorable results were described by various observers in anemia and chlorosis, although this is difficult to understand since the red bone marrow is stimulated not by raised atmospheric pressure but rather by pressures less than 1 atmosphere. (See Hoff and Fulton (*3*) 1942, references no. 1501 to 1808; and Hoff, Hoff, and Fulton (*4*) 1944, references no. 6215 to 6234.) For observations on the use of pressure chamber therapy in anemia, the reader should consult the papers by the following investigators: Pravaz (*2583*, *2584*, *2585*) 1840 and 1841, Milliet (*2607*) 1855, Sandahl (*2701*, *2702*) 1867 and 1869, Gent (*2662*) 1869, von Liebig (*2681*, *2682*, *2683*) 1872, 1875 and 1877, Canuet (*2650*) 1873, Féréol (*2656*) 1873, Lange (*2673*) 1876, Bordier (*2643*) 1877, Lessdorf (*2678*) 1881, Fyan (*2661*) 1882, Arntzenius (*2559*) 1887, and Thompson (*2707*) 1889.

Pressure chamber therapy in heart diseases has been a controversial issue in the past. Storch (*2705*) 1865 recommended it in mitral insufficiency and Sandahl (*2701*) 1867 believed that in this condition raised pressure had a palliative effect. Levinstein (*2679*) 1864 considered aortic stenosis an indication for pressure chamber treatment and von Liebig, 1883 (*2685*) used it in any cases of compensated heart disease. However, Charrier (*2651*) 1880 believed that patients with valvular lesions should not be subjected to raised atmospheric pressures. Blumauer (*2614*) 1940 listed as contraindications to pneumatic pressure chamber therapy, acute pyrexial diseases, hypertension, and circulatory failure. Pravaz's paper (*2581*) 1837–38 referred to beneficial effects in epistaxis and Mayer (*2690*) 1869 alluded to its use in ascites.

From earliest times, it has been noted that certain individuals descending to the sea bottom in diving bells experience improvement in hearing while under the influence of raised atmospheric pressure and this led to the expectation that pressure chambers might be of value in treating ear disturbances. Cases of otorrhea were treated in the pressure chamber by Pravaz (*2583*) 1840 and obstructions of the Eustachian tube were similarly treated by Warden (*2709*) 1848–49. Pressure chamber treatment of catarrhal deafness was referred to by Pravaz (*2581*, *2582*, *2583*, *2584*, *2585*)

1837–38, 1840, and 1841, Levinstein (*2679*) 1864, Freud (*2659*) 1866, Bertin (*2642*) 1866, Sandahl (2701) 1867, and Bordier (*2643*) 1877. In 1865, Smoler (*2704*) commented on the effect of diving in improving auditory acuity and caisson workers and divers have from time to time called attention to increased acuity while under pressure. However, there is little evidence that permanent improvement in hearing can be achieved by subjecting patients to raised atmospheric pressures.

With regard to digestive and metabolic diseases, the evidence for beneficial effects of raised atmospheric pressures is of doubtful value. Lee (*2605*) 1867 recommended the use of the pressure chamber in dyspepsia; Pravaz (*2581*, *2582*, *2583*, *2584*) 1837–38 and 1840 claimed good results in anorexia. Pravaz also considered the treatment of value in convalescence from cholera and used the pressure chamber in malnutrition. Pressure chamber therapy was used by Kelemen (*2669*) in 1879 as a diuretic, and diabetics were subjected to increased atmospheric pressures by Sandahl (*2699*, *2700*) 1865 and Moeller (*2691*, *2692*) 1881. These workers did not consider that pressure chamber treatment was a specific cure for diabetes mellitus although some reduction in urinary output and urinary glucose was claimed. Storch (*2705*) 1865 referred to pressure therapy in Bright's disease and Charrier (*2651*) 1880 described the cases of two middle-aged obese women, both of whom showed some weight loss as a result of pneumatic chamber treatments.

Various gynecological conditions have been treated in the past in compressed air chambers. Lee (*2605*) 1867 referred to the treatment of amenorrhea in the chamber. Benefit in menorrhagia was claimed by Pravaz (*2581*, *2582*, *2583*, *2584*)) 1837–38 and 1840. Irregular menstruation was believed to be corrected by pressure therapy, according to Bertin (*2640*) 1855 and Sandahl (*2701*) 1867. Lange (*2673*) 1876 alluded to treatment of vaginal "inflammation" and according to von Liebig (*2685*) 1883, cases of persistent leucorrhea were successfully treated by sessions in the pressure chamber.

A number of other acute and chronic conditions have been subjected to pressure chamber treatment. These are mentioned to indicate the tremendous popularity which the compressed air "bath" enjoyed in continental Europe in the nineteenth century. Lee (*2605*) 1867, Lange (*2673*) 1876, Moeller (*2691*, *2692*) 1881, and von Liebig (*2685*) 1883 treated cases of persistent neuralgic pain by pneumatic methods. Chorea was treated by Lange (*2673*) 1876. Lee (*2605*) in 1867 used the chamber in hypochrondriasis and Lange (*2673*) 1876 reported the use of the pressure chamber in hysteria. Conjunctivitis was treated by Pravaz (*2583*, *2584*) 1840. Brodowskiego (*2645*) 1866 and Lange (*2673*) 1876 also considered the treatment of value in eczema. The most far-fetched indications are those of Caffe (*2648*) 1863—viper bites and smallpox!

No discussion of the possible therapeutic effects of raised atmospheric pressures would be complete without reference to the so-called "tank treatment" practiced by Cunningham. An analysis of this treatment appeared in 1928 (*2712*). Patients were subjected to raised atmospheric pressures in a chamber. Claims for this treatment included cure of syphilis, pernicious anemia, and diabetes mellitus. Cunningham regarded the method as a practical and efficient way of administering oxygen and claimed temporary beneficial results in high blood pressure, acidosis, and conditions requiring support of the heart. Relief was claimed also in the pains of tabes dorsalis. It appears that treatment of malignant disease was also undertaken. A consideration of the literature which has been discussed in this section will serve to make clear to the reader the fallacies of some features of the Cunningham treatment.

The use of diminished atmospheric pressure has been referred to in relation to the treatment of pertussis. Readers who wish to investigate further the literature on the therapeutic action of high altitudes may consult references in Hoff and Fulton (*3*) 1942 (references no. 4911 to 5028) and Hoff, Hoff, and Fulton (*4*) 1944 (references no. 7478 to 7490).

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E. USES OF COMPRESSION CHAMBERS IN THE ADMINISTRATION OF NITROUS OXIDE AND DRUGS

In the use of nitrous oxide as an anesthetic, a difficulty early encountered was that of supplying the gas under sufficient tension to produce anesthesia and yet maintain an adequate oxygen pressure to satisfy the respiratory demands and prevent asphyxia. As a solution to this problem, Bert (*16*) 1878 conceived the idea of inducing anesthesia with nitrous oxide at a pressure higher than 1 atmosphere.

Fontaine (*2716*) 1879 constructed a mobile chamber capable of holding 15 to 20 persons in which anesthesia could be induced and surgical operations carried out. By 1879, 27 patients had been operated upon in this chamber under pressures of one-fourth to one-third of an atmosphere above normal. It was claimed that cyanosis and asphyxia were absent and that when the mask was removed at the end of the operation, consciousness quickly returned. Among the advantages claimed for this method were its safety and the uniformity of the anesthesia. Post-anesthetic excitement and vomiting were stated to be suppressed. Fontaine recommended the use of the chamber to facilitate the reduction of hernias and patients with asthma, emphysema, chronic bronchitis, and anemia were also treated. A large pressurized surgical amphitheater was contemplated which would have a capacity such that students and other observers could all be present within the pressurized atmosphere. (See Amelot (*2713*) 1880.) Amelot (*2713*) also alluded to a description by Prosper Merimé in his *Lettres à une inconnue* of a therapeutic chamber in which Merimé himself was a patient. For many obvious reasons, the administration of nitrous oxide under raised atmospheric pressure has now become unnecessary and has long since been discontinued.

Not only has increased atmospheric pressure been suggested to potentiate the action of volatile drugs, but also it has been recommended to enhance and prolong the action of certain other therapeutic agents, particularly those acting upon the central nervous system. Corning (*2714*, *2715*) 1891 and 1903 found that such drugs as strychnine, potassium bromide, alcohol, sulfonal, and colchicine apparently exert a more profound and continued action in patients kept under 2 atmospheres (absolute) than in those in ambient air. Corning's paper published in 1903 contains a synopsis of his experiences in applying this method over 6,000 times.

2713. Amelot, [ ]. Note sur l'aérothérapie et l'emploi chirurgical de l'air comprimé. *Rev. Thér. méd.-chir.*, 1880, *47:* 9–13. [R]

2714. Corning, J. L. The use of compressed air in conjunction with medicinal solutions in the treatment of nervous and mental affections. *Med. Rec., N. Y.*, 1891, *40:* 225–232. [R]

2715. Corning, J. L. The use of compressed air to enhance and prolong the action of remedies upon the cerebrospinal axis: synopsis of experiences in applying the method over six thousand times. *Amer. Med.*, 1903, *5:* 529–532. [R]

2716. Fontaine, J.-A. Emploi chirurgical de l'air comprimé. *Un. méd., Paris*, 1879, Sér. 3, *28:* 445–448. [C, P]

2717. Hassall, A. H. On the principles of the construction of chambers for inhalation in diseases of the lungs. *Brit. med. J.*, 1884, *1:* 46–47. [R]

2718. Hawley, G. F. A new apparatus for nebulizing nonvolatile medicaments and for administering the same through impacted air, as a medium, by the process of forced dilatation, instead of by inhalation, spray, or douche. *J. Amer. med. Ass.*, 1894, *22:* 702–705.

II. DIFFERENTIAL PNEUMATOTHERAPY (RESPIRATION OF COMPRESSED AND RAREFIED AIR)

A. HISTORY OF TREATMENT BY RESPIRATION OF COMPRESSED AND RAREFIED AIR

Closely allied to the method of treating patients by subjecting them to raised atmospheric pressures in the compression chamber is the technique of so-called differential pneumatotherapy. In this procedure, the patient remains at normal atmosphere breathing compressed or rarefied air by means of an airtight face mask. Inclusion and discussion of the literature on the physiological effects and therapeutic value of this procedure may not be inappropriate since the findings bear relationship to the use of resuscitators and artificial respirators as well as to pressure breathing at high altitudes and respiration in the "lung" during individual escapes from submerged submarines.

The earliest reference to pressure breathing in therapy is a report by Steinbrenner (*2761*) who in 1840 described an iron drum of about 2 liters' capacity, partially filled with water, by means of which a resistance to inspiration and expiration was provided. Breathing with this device was stated to increase vital capacity, and it was recommended in the prevention and treatment of pulmonary tuberculosis. Rose (*2751*) 1875 referred to a differential pneumatic apparatus in use in St. Petersburg about 1868.

The first portable pneumatic apparatus was developed by Hauke in Vienna in 1870 (See Solis-Cohen (*2755*) 1887). This instrument was essentially a gasometer in which the pressure of the contained air could be raised above the ambient atmosphere or lowered to a level below an atmosphere by altering a water-level. Patients could inspire or expire compressed air or rarefied air in any desired combination. Hauke recommended inspiration of compressed air in the prevention of tuberculosis and expiration of the rarefied air in the treatment of emphysema. Hauke also devised an airtight cuirasse which fitted on the chest. By alternate compression and rarefaction of the air in this device, the chest could be expanded and compressed and artificial respiration maintained. In another apparatus devised by Hauke, the patient was placed in an airtight cabinet with the head projecting from the top. A collar around the neck prevented escape or entry of air. The patient breathed atmospheric air and a differential pressure was created by compressing or rarefying the air in the chamber. A modification of this apparatus was the pneumatic differentiation cabinet devised by Ketchum (*2863*) 1886 and introduced for therapeutic purposes by Williams (*2876*) 1885. Literature on this chamber is reviewed in the section on pneumatic differentiation (page 330).

Hauke's gasometer for providing compressed or rarefied air was used by Waldenburg in Berlin as a therapeutic procedure. In 1873, Waldenburg (*2768*) designed a spirometer of his own by means of which patients could breathe condensed or rarefied air. The apparatus consisted of an inner and an outer cylinder, each 1 m. high, the inner cylinder being 27 cm. in diameter, and the outer cylinder 30 cm. The device was filled with water to a height of about 20 cm. Weights could be attached to cords on a pulley system so that the inner cylinder could be drawn up and the contained air rarefied. Attaching a net weight of 20 lb. produced a rarefaction of the air of about one-sixtieth of 1 atmosphere. The pressure could be measured accurately on a mercury manometer. To produce compressed air, it was only necessary to add weights to the top of the cylinder, a 10 lb. weight producing a compression of one-sixtieth of an atmosphere. A flexible tube led from the cylinder to a face mask provided with a 3-way valve so that the patient could breathe either compressed or rarefied air. Waldenburg used differential pressures of one-sixtieth to one-fortieth of an atmosphere and after patients became adapted, went as high as one-twentieth of an

atmosphere. Inspiration of condensed air was stated to diminish the amount of blood in the lungs, to reduce blood pressure and the pulse rate. Expiration into condensed air produced the same effects. Inspiration of rarefied air tended to increase the amount of blood in the lesser circulation. Expiration into rarefied air had a similar but lesser action.

A further description of Waldenburg's apparatus appeared in 1875 (*2769*) and in 1880, Waldenburg (*2770*) published a large 618-page monograph on the management of respiratory and circulatory diseases with the apparatus. This monograph is the definitive volume on this subject and contains a description of the physiological action of the Waldenburg apparatus and a comparison of its effects with those of the therapeutic pressure chamber. Indications for treatment are also laid down in great detail. Waldenburg was led to the use of differential pneumatotherapy as a result of his studies on expiratory and inspiratory force and volume as a means of diagnosis in various respiratory diseases. He claimed that in certain diseases such as emphysema, inspiratory power may be normal or nearly so. In advanced pulmonary tuberculosis, both inspiration and expiration may suffer changes. Because of these considerations, it occurred to him that a therapeutic procedure should be capable of acting separately on inspiration and expiration.

Other descriptions of Waldenburg's apparatus and its uses were published by Lange (*2744*) 1876, Spillmann (*2760*) 1876, and Forlanini (*2732*) 1878–79. Forlanini operated the apparatus at a positive pressure of 15 mm. Hg. Cramer (*2724*, *2725*) 1884 and 1885 described a new model of the Waldenburg apparatus from which patients breathed air under a positive pressure of 20 to 25 mm. Hg and a negative pressure of 35 to 40 mm. Hg. Pircher (*2749*) 1876 used the Waldenburg apparatus in conjunction with a pressure chamber in the management of emphysema. Patients exhaled into a negative pressure of one-sixtieth of an atmosphere.

For more detailed discussions of the historical aspects of differential pneumatotherapy the reader may consult reports by Waldenburg (*2799*) 1874, Rose (*2751*) 1875, Pramberger (*2750*) 1879, Lépine (*2745*) 1875, and Solis-Cohen (*2755*, *2756*) 1887.

Many modifications of the Waldenburg apparatus have been described in the literature and other devices for delivering compressed or rarefied air based on different principles have been developed and used. Biedert (*2720*) in 1874 described a respirator which was essentially a bellows by which air could be compressed or rarefied. The patient could either inhale or exhale under conditions of rarefied or compressed air and any combination of differential pressures could be used. Wolff (*2771*) 1876 used Biedert's apparatus with apparently satisfactory results in emphysema, bronchitis, and mitral and tricuspid insufficiency. A report of inspiratory and expiratory pressure in patients with emphysema and bronchial asthma was given by Biedert in 1880 (*2722*). Fränkel (*2736*) 1875 described an accordian-like apparatus which was essentially similar in principle to the apparatus designed by Biedert. Modified apparatuses for pressure breathing were also described by Clar 1886 (*2723*), von Cube (*2726*) 1874, and Evler (*2728*) 1906. The latter's apparatus delivered air under a pressure of 10 to 30 mm. Hg. The device was used in the treatment of asthma and various medicaments were also added to the air. Fleischer's apparatus, described in 1887 (*2729*, *2730*) permitted inspiration of compressed air and expiration into rarefied air. It was used in emphysema, asthma, and valvular heart disease with cyanosis, edema, or dyspnea. Fleischer recommended several sessions a day, each lasting at least 10 to 15 minutes. The apparatus delivered differential pressures of one-fiftieth to one-thirtieth of an atmosphere above or below normal pressure. Fleischer's apparatus was essentially a pump operated by a running stream of water. The apparatus could run continuously. A modification of the Waldenburg apparatus was also described by Forlanini (*2733*, *2734*) 1880 and 1889. Compressed air at pressures of 10 to 40 mm. Hg above 1 atmosphere or 20 to 40 mm. Hg below 1 atmosphere could be provided.

A continuously acting, transportable pneu-

matic apparatus was described by Geigel (*2737*) 1876. Högyes (*2741*) 1874 described a device with both a positive and a suction action. Other devices were described by von Liebig (*2746*) 1880, Schnitzler (*2752*, *2753*) 1874 and 1876 and by Solis-Cohen (*2754*, *2755*) 1884 and 1887. Solis-Cohen's apparatus was essentially a gasometer combined with a foot bellows and was capable of continuous action. It delivered air under positive pressures of one-seventieth to one-fortieth of an atmosphere. It was considered unsafe to go above one-eightieth to one-sixtieth of an atmosphere differential pressure, at first, but after the patient became adapted, pressures of one-fortieth of an atmosphere above normal could be tolerated. Positive pressures exceeding one-thirtieth of an atmosphere were never used. The technique was used in early cases of phthisis, chronic bronchitis, partial lung collapse after pneumonia, and all cases in which it was desired to increase vital capacity. Expiration into rarefied air was used in emphysema. The air delivered to the patient could be dried and warmed and medicaments could be added to the airstream. The apparatus could be used for inspiration of compressed air, inspiration of rarefied air, expiration into compressed air, expiration into rarefied air, inspiration of compressed air plus expiration into compressed air, inspiration of rarefied air plus expiration into rarefied air, inspiration of compressed air plus expiration into rarefied air, or inspiration of rarefied air plus expiration into compressed air. In describing his apparatus for pneumatic treatments in hospitals in 1889, Solis-Cohen (*2758*) 1889 reported that 12 patients could be treated at a time, each patient being given 2 sets of inhalations a day.

Störk's apparatus (*2762*, *2763*, *2764*) described in 1874, was operated so as to deliver compressed air at a pressure of 15 to 20 mm. Hg. The differential pressure never exceeded 40 mm. Hg. This apparatus was criticized by Schnitzler (see Störk (*2763*) 1874), who claimed that the patient rebreathed his own carbon dioxide-laden air. A portable pneumatic apparatus, described in 1883 by Wagner (*2767*) embodied no new design but was simply an improvement of the Waldenburg apparatus.

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2722. Biedert, [ ] Die Methoden der Pneumatometrie und die Theorien des Emphsem und des Bronchialasthma. *Berl. klin. Wschr.*, 1880, *17:* 258–262. [P]

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2727. Cube, [ ] von. Der pneumatische Doppel-Apparat und das kombinirte Verfahren bei der mechanischen Behandlung der Respirationsorgane. *Wien. med. Wschr.*, 1874, *24:* 617–619; 638–641. [P]

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2730. Fleischer, R. Ueber einen neuen pneumatischen Apparat zur Einathmung comprimirter und zur Ausathmung in verdünnte Luft. *Münch. med. Wschr.*, 1887, *34:* 585–587. [P]

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2733. Forlanini, C. Di alcune modificazioni all-apparato pneumatico trasportabile di Waldenburg. *Gazz. Osp. Clin.*, 1880, *1:* 3–13. [P]

2734. Forlanini, C. Nuovi apparati pneumatici trasportabili. *Morgagni*, 1889, *31:* 257–299. [P]

2735. Fränkel, B. Ein einfacher pneumatischer Apparat. *Zbl. med. Wiss.*, 1874, *12:* 693–694. [P]

2736. Fränkel, B. Ein billiger pneumatischer Apparat. *Berl. klin. Wschr.*, 1875, *12:* 252–255. [P]

2737. Geigel, [ ]. Vorläufige Mittheilung über einen continuirlich wirkenden, transportablen pneumatischen Apparat mit neuem mechanischem Princip. *Dtsch. med. Wschr.*, 1876, *2:* 257. [P]

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B. PHYSIOLOGICAL EFFECTS OF BREATHING COMPRESSED AND RAREFIED AIR

Waldenburg (*2798*, *2799*) 1873 and 1874 found that inspiration of condensed air and expiration into rarefied air, using differential pressures between one-sixtieth and one-fortieth of an atmosphere, increased ventilation for a time. There was a persistent increase in vital capacity. However, Lebegott (*2790*) 1882, in referring to the therapeutic effects of expiration into rarefied air in the Waldenburg apparatus, stated that vital capacity is not increased, that expiratory volume becomes less and less, and the duration of a single expiration becomes less with the reduction of pressure. Waldenburg measured the inspiratory and expiratory forces and stated that both were increased by use of the pneumatic apparatus. Inspiration of rarefied air was used in emphysema in which there was a definite increase in expiratory force after treatment. With inspiration of compressed air, the pressure in the lungs became less negative or even positive. There was a tendency toward reduction in the amount of blood in the pulmonary circulation. This finding was also reported by Bagna (*2774*) 1880 and Cavallero (*2777*) 1889. The opposite effects were noted on inspiration of rarefied air. The pressure in the lungs became more strongly negative and there was an increase of blood in the thorax. Similar but less marked effects were found on expiration into rarefied air.

Solis-Cohen (*2755*, *2756*) 1887 stated that the effects of differential pressure varied with the degree of pressure and the time during which the process was continued. In his procedure, differential pressures of one-eightieth to one-thirtieth of an atmosphere were used for 10 minutes to one-half hour. Inspiration of compressed air led to greater expansion of the lungs, slower respiration and a gradual increase of vital capacity. Pulmonary hyperemia was stated to be relieved and pathological secretions in the lungs dislodged. Expiration into compressed air resulted in greater expiratory excursions and effects on the circulation comparable to those produced by inspiration of compressed air. Inspiration of rarefied air at a differential pressure of one-sixtieth of an atmosphere increased the effort required to expand the chest, but if the effort could be made, the elasticity of the lungs was stated to be increased. Ventilation, on the whole, was increased. The final effect on the circulation was an increase of blood pressure. Expiration into rarefied air at a pressure differential of one-sixtieth to one-twenty-fourth of an atmosphere facilitated contraction of the thorax. Ventilation and gaseous exchange were subsequently increased because subsequent inspirations became easier and deeper. There was an increase in vital capacity. Circulatory effects were similar to those noted on inspiration of rarefied air but more marked. There was a tendency to pulmonary congestion. The effect of alternate inspiration of compressed air and expiration into rarefied air was an increase in pulmonary ventilation and relief of hyperemia in the lungs, if present. Inspiration of rarefied air and expiration into compressed air increased the muscular effort necessary to complete each respiratory act and respirations were prolonged. Inspiration of rarefied air increased the effort of inspiration and facilitated and hastened expiration. There was a reduction in blood pressure.

Reporting on the effect of compressed and rarefied air on healthy human subjects, Lenzmann (*2791*) 1881–82 stated that inspiration of compressed air produced essentially the same effects upon the circulation as the Valsalva maneuver. The blood pressure fell, the pulse was accelerated for several minutes and then gradually returned to normal. Sometimes, there was a supernormal phase before the blood pressure returned to normal. In subjects exhaling into compressed air, the blood pressure also fell, with sometimes a supernormal phase before return to normal. The pulse rate was also accelerated during the experiment. Inspiration of rarefied air resulted in a rise of blood pressure. On prolonged breathing of rarefied air, the blood

pressure sometimes remained unchanged or fell, but there was always an after-phase of elevated blood pressure. Expiration into rarefied air produced the same effects. Drosdoff (*2781*) 1875 also found that breathing air under positive pressure (one-sixtieth of an atmosphere) lowered the blood pressure.

Experiments carried out on dogs by Gréhant and Quinquad (*2784*) 1884 showed that pulmonary insufflation with air under a pressure of 35 mm. Hg caused a fall in arterial blood pressure from 120 mm. Hg before the experiment to 70 mm. Hg during the experiment. Compressed air at a pressure of 10 mm. Hg lowered the blood pressure by 4 mm. Hg. Death resulted 5½ minutes after insufflation of air at 80 mm. Hg and bubbles of air were found in the carotid arteries within 1½ minutes. At 65 mm. Hg air bubbles were seen in the arteries in 3 minutes. In a rabbit, compressed air at a positive pressure of 30 mm. Hg caused a fall in blood pressure and bubbles were seen in the arteries in 1¾ minutes.

Other studies on the physiological effects of compressed and rarefied air were carried out by Riegel and Frank (*2794*) 1876, Küss (*2789*) 1877, Forlanini (*2783*) 1878-79, de Jager (*2786*) 1885, Kelemen (*2788*) 1886, Bass (*2775*) 1926, and Diener (*2616*) 1936.

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C. INDICATIONS FOR TREATMENT WITH COMPRESSED AND RAREFIED AIR

There is general agreement in the early literature as to the indications for respiration of compressed or rarefied air. These indications were set forth in a paper by Solis-Cohen (*2755*) in 1887. Respiration of compressed air was recommended by him in laryngeal and tracheal stenosis, chronic bronchitis, atelectasis, pleurisy (either with or without effusion), and early pulmonary tuberculosis. The basis for treatment rested upon the action of compressed air in opening disused alveoli, increasing vital capacity, relieving pulmonary congestion, and increasing oxygenation. For these reasons, the procedure was also recommended in anemia. Compressed air was also recommended in asthma, using a differential pressure of one-thirtieth of an atmosphere. In asthma, however, best results were usually obtained by expiration into rarefied air. Compressed air was recommended in pulmonary hemorrhage by some authors, but Solis-Cohen considered that the method might be dangerous.

For a discussion of the use of respiration of compressed air in chronic respiratory diseases, the reader should consult Waldenburg's paper (*2846*) published in 1874. Waldenburg also recommended inspiration of compressed air in cases of insufficiency or stenosis of the mitral and aortic valves. However, Solis-Cohen (*2755*) 1887 claimed to have had no experience with the method in cardiac lesions and some authors believed that respiration of air at differential pressures was contraindicated in cases of valvular heart disease.

Inspiration of compressed air with expiration into the rarefied air was stated by Solis-Cohen to be indicated in cases in which it was desired to increase gaseous exchange. Waldenburg (*2847*) 1875 recommended inspiration of rarefied air in stenosis or insufficiency of the valves of the right side of the heart. Expiration into compressed air was believed to act as a gymnastic measure to strengthen the respiratory muscles as did also inspiration into rarefied air alone. The latter is sometimes useful, according to Solis-Cohen (*2755*) 1887, in emphysema. For asthma with expiratory difficulty, relief was obtained by expiration into rarefied air.

For further discussions of the indications for compressed and rarefied air, the reader may consult papers by Schnitzler (*2832*) 1875, Schuppert (*2835*) 1875-76, Caruso (*2804*) 1882, Waldenburg (*2848*) 1880, Kyner (*2821*) 1887-88, and Solis-Cohen (*2759*) 1889. The last four papers contain case reports.

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2811. Edlund, E. Om Prof. Waldenburg's transportabla pneumatiska apparater. *Hygiea, Stockh.*, 1879, *41:* 295–298. [R]

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2815. Haenisch, F. Zur Wirksamkeit der pneumatischen Behandlungsmethode. *Dtsch. Arch. klin. Med.*, 1874, *14:* 445–454. [P, R]

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2833. Schoube, [ ]. Den mekaniske Behandling af Aandedraets- og Kredslbsorganernes Sygdomme. *Ugeskr. Laeg.*, 1877, *23:* 177–185; 193–204. [R]

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III. PNEUMATIC DIFFERENTIATION

Reference has already been made to the so-called "Wärme" or "tub" constructed and operated by Hauke (*2740*) 1872. This was an airtight cabinet of sufficient size to contain a recumbent patient. It was fitted with a rubber cover which encircled the neck of the patient and fastened around the upper edge of the cabinet itself. The patient's body was thus enclosed in an airtight container while the head was outside. Air could be exhausted from the interior and so inspiration facilitated. If the air were compressed around the body, the expiratory phase of respiration was made easier. Bowditch (*2853, 2854*) 1885 referred to the Hauke "Wärme" and mentioned also another device based on the same principle. This was known as the "Hadfield Body Receiver for the New Haven Vacuum Cure" which was in use by an irregular practitioner in 1869.

The major development of the Hauke principle in America was the technique of "pneumatic differentiation" initiated by Williams (*2876*) 1885. In this method of treatment, the patient was placed in a small airtight cabinet. Within it, the air could be compressed or rarefied as desired. Differential pressure breathing could be effected by having the patient breathe room air through a tube leading into the cabinet from the exterior. This pneumatic differentiation cabinet, which was designed by Ketchum (*2863*) 1886, was a safe-like structure constructed of iron with a large thick window at one end. It was 6 to 7 ft. high, 3 ft. wide, and 3½ to 4 ft. long. Opposite the window, there was an iron door edged with rubber. The patient sat on a chair within the cabinet, facing the window. Passing through this window, there was a short rubber tube, 1½ inches in diameter, with a stop-cock outside and ending on the outside in a funnel-shaped opening through which medicinal sprays could be added to the air as desired. At the inner end of the tube, a mouthpiece for the patient was provided.

Under one condition of use of the device, the patient was placed in the interior with the stop-cock closed and the air rarefied by approximately 5 mm. Hg. The patient then placed the tube in his mouth, the nose being closed by a clip, and the stop-cock was opened. He thus made a forced inspiration. He could also exhale against the pressure and when he was fatigued, the stop-cock could be closed and he could breathe the air within the cabinet. A number of medicated sprays containing phenol, iodine, iodoform, bichloride of mercury, or other substances could be introduced. Many combinations of differential pressure breathing could be used by compressing or rarefying the air in the cabinet or by alternate compression and rarefaction with expiration and inspiration. Each treatment usually lasted about 10 to 30 minutes. They were usually given daily and patients were subjected to as many as 135 sessions in the cabinet. At the onset of treatment, pressure

differentials of more than 2.5 to 5 mm. Hg were not used but during the session it was safe to increase the differentiation gradually to 25 mm. Hg or more.

According to Williams (*2879*) 1887, the technique of pneumatic differentiation consisted of the following respiratory procedures: (*a*) forced inspiration, (*b*) inspiratory differentiation, (*c*) respiratory differentiation, (*d*) expiratory differentiation, (*e*) forced expiration, (*f*) residual air expansion, and (*g*) residual air compression. In forced inspiration, the valves were set for rarefaction of the cabinet and the patient inspired outside air from the tube with the cabinet decompressed by 5 to 50 mm. Hg. He exhaled into the cabinet. In the procedure of inspiratory differentiation, the cabinet remained decompressed while the patient inhaled and exhaled through the tube. By this latter procedure, inspiration became passive while expiration was the active phase. The intrathoracic pressure was increased and the air passages and alveoli were distended. The procedure exercised and strengthened the muscles of expiration, but Platt (*2869*) 1886 stated that the continued pressure might cause permanent emphysema. Blood flow from the thorax into the extrathoracic portion of the vascular system was increased and this tended to promote relief of local plethora and congestion of the lungs.

In the procedure of respiratory differentiation, the valves of the cabinet were set for alternate rarefaction and compression. As the patient breathed in the outside air through the tube, the cabinet was rarefied; as he exhaled through the tube into the outside air, the cabinet was compressed. Used in this way, the device was actually an artificial respirator and acted to increase lung ventilation. In expiratory differentiation, the chamber was compressed and the patient inspired and exhaled through the tube. Under these conditions, the inspiratory effort was increased, whereas expiration was made easier. With this procedure, there was a tendency toward increased flow of blood into the thorax and it was stated by Platt that the lungs might be subjected to local plethora with a possibility of congestion and hemorrhage. The arterial blood pressure tended to be increased. In forced expiration, the cabinet was compressed and the patient inspired from the cabinet air with the stop-cock of the breathing tube closed and then exhaled through the tube into the outside air. In the procedures of residual air expansion and residual air compression, the patient made a full inspiration within the cabinet which was then decompressed or compressed by 25 to 50 mm. Hg, producing rapid expansion or compression of the air within the lungs.

Williams (*2879*) 1887 recommended respiratory differentiation as a means of respiratory calisthenics. By expiratory differentiation the inspiratory muscles were strengthened, whereas inspiratory differentiation produced the opposite effect of strengthening the expiratory muscles. For this purpose, differential pressures of 5 to 10 mm. Hg were recommended. In complicated cases of emphysema, expiratory differentiation and forced expiration were used. When complicating bronchial catarrh was present, the treatments might be interspersed by inspiratory differentiation or forced inspiration at a vacuum of 5 to 10 mm. Hg for the purpose of applying appropriate remedial agents in the form of spray. For bronchiectasis, Williams recommended expiratory differentiation and forced expiration with fairly high pressures. Cases of simple laryngitis, tracheitis and bronchitis were treated by inspiratory differentiation and forced inspiration with a vacuum of 5 to 10 mm. Hg. For asthma, Williams used forced inspiration or respiratory differentiation. Inspiratory differentiation was also used but it was found that too great a pressure differential might cause a bronchial spasm. Williams also noted that anemia, chlorosis, and some forms of heart diseases were benefited by the use of inspiratory differentiation.

Williams regarded inspiratory differentiation as a particularly valuable method for introducing medicaments. The forced inspiration, he believed, carried the medicated air far into the lung passages, while on exhaling against a resistance, vapors tended to condense upon the respiratory surfaces. Several authors have called attention to the fallacy of

this aspect of the treatment. In the first place, it is very doubtful whether the antiseptic substances used were carried beyond the bronchioles; second, they could not, in any case, come in contact with the active lesions, for example, in tuberculosis; third, there is grave doubt as to whether they would have been effective had they actually come in contact with the diseased tissue; and finally, since they were present in the lungs in the form of a finely divided spray and not in vaporized form, there was no reason why an increase in intrapulmonary pressure should cause them to condense.

A larger problem concerning the technique of pneumatic differentiation was its value in pulmonary tuberculosis. Williams believed that benefit was obtained from inspiratory differentiation (at a differential of 5 to 15 mm. Hg) for 5 to 10 minutes, once or twice a week. In some early cases of tuberculosis, he advised daily treatments of 10 to 20 minutes until there was symptomatic improvement. In long-standing cases he gave daily treatments for a week or 10 days and then weekly or biweekly treatments over months or years. Williams (*2876*) 1885 stated that he had never observed hemorrhage as a result of such treatment. Improvement of symptoms was reported in three cases of emphysema. Williams (*2877*, *2878*) 1886 also described cases of pulmonary tuberculosis which appeared temporarily improved by therapy with pneumatic differentiation. Generally, the case histories indicated relief of symptoms only, the chest signs remaining unchanged. It is impossible to make an appraisal of the course of the pathological process since X-rays were not available. However, Williams checked the sputum for acid-fast bacilli in some cases. It is quite clear even from Williams' cases, that pneumatic differentiation therapy did not cure tuberculosis.

Platt (*2869*, *2870*) 1886 criticized Williams' use of medicated sprays claiming that little, if any, of the sprays used penetrated deeply into the air passages and that the substances would not condense since they were in the form of a finely divided mist and did not saturate the air.

Regarding the physiological action of inspiratory differentiation, Donaldson (*2859*) 1885-86 reported in human subjects an increase of 20 to 100 percent in respiratory uptake and a persistent increase in chest expansion. It was claimed that the procedure facilitated flow of blood from the lungs to the left heart and that oxygenation of the blood was enhanced. In experiments on chloralosed rabbits, Martin and Donaldson (*2865*, *2866*) 1886 found that in animals breathing air from the outside with the cabinet decompressed, there was a fall in blood pressure with a subsequent supernormal phase afterwards. There was little change in the pulse rate and if the animal breathed air from within the cabinet only, no essential change in the blood pressure occurred. In animals breathing air from the outside with the cabinet compressed, the blood pressure showed transient but considerable rise.

Clinical investigations by Bowditch (*2853*, *2854*, *2855*, *2856*) 1885 and 1886 were carried out in an attempt to evaluate the use of pneumatic differentiation in respiratory diseases. Twenty-seven cases of pulmonary tuberculosis, acute and chronic bronchitis, and asthma were treated. Of these, Bowditch reported no benefit in 5 cases, slight or temporary benefit in 6 cases, marked improvement in 12 cases, remarkable improvement in 2 cases, and a cure in 1 case. Nineteen of these cases were described as having tuberculosis or "incipient tuberculosis." Of these, 6 experienced little or no benefit, 4 were described as having received temporary benefit, 3 were improved, 6 received marked benefit for several months, and 1 was claimed as "cure." This patient was, however, a so-called "incipient" case. Bowditch gave formulas for various sprays for use with the method, but he, like Platt, was skeptical of their value. He had 4 cases in which hemorrhage occurred during treatment or immediately after. Bowditch's papers (*2855*, *2856*) published in 1886, should be consulted for detailed histories. It is difficult to appraise them accurately but again one is impressed by the failure of the treatment to produce lasting improvement in tuberculosis.

Houghton (*2861*) 1885 recommended pneumatic differentiation to strengthen and expand the lungs, to arrest early pulmonary disease and to prolong life and increase comfort in the latter stages of pulmonary disease when cure was impossible. Houghton concluded that in tuberculosis, pneumatic differentiation may be of service in certain cases and that expansion of the lungs is in itself a therapeutic measure of merit. He believed that if there was no improvement as a result of the first 10 to 12 applications, continued use of the treatment was of questionable value or might even be contraindicated.

Improvement in the case of a boy of 14 years of age with night sweats, loss of weight, and afternoon temperature was reported by Jensen (*2862*) 1885. However, Moeller (*2868*) 1886 was skeptical of reported cures of pulmonary tuberculosis. He called attention to the fact that Waldenburg at first used medicinal sprays in connection with his apparatus but subsequently abandoned this therapy. Moeller also pointed out that Williams' apparent cures in tuberculosis lacked bacteriological confirmation as to diagnosis or cure. With regard to asthma, Moeller believed that the method may improve the condition, but that cure could not be insured unless the underlying causes were removed. He believed that pulmonary differentiation was really of value in emphysema, pleuritic adhesions, and pulmonary engorgement. In chronic bronchitis, the method was most successful in the serous, nonpurulent forms. In tuberculosis, the method should, according to Moeller, be considered as palliative only.

In 1886, Fox (*2860*) reported 69 cases of asthma, acute bronchitis, chronic bronchitis, pyothorax, pulmonary tuberculosis, and other conditions treated by pneumatic differentiation. Of these, 27 recovered, 21 were reported as improved, 13 were not improved, and 8 died. In all cases, at least a year had elapsed since treatment. Twenty-three cases of acute bronchitis were treated and all were reported as having recovered. There were 34 cases of pulmonary tuberculosis, of which 17 were considered improved and 10 not improved. Seven of these died. Apparently the treatment gave some symptomatic relief to most sufferers from tuberculosis.

For further case reports of the use of pneumatic differentiation in respiratory disease, the reader may consult papers by Von Ruck (*2873*, *2874*) 1886 and 1888. In the latter paper, a synopsis is given of results in 92 cases. In 32 cases stated to be early tuberculosis, 21 were reported as recovered, 9 as improved, and 2 still under treatment and making progress. In 26 cases diagnosed as more advanced pulmonary tuberculosis, 3 were considered recovered, 9 were claimed to be arrested, 4 were to some extent improved, while 8 showed little or no improvement and 2 were still under treatment. In 12 cases of chronic bronchitis, 8 were completely recovered and 4 greatly or moderately improved. Improvement was also claimed in cases of bronchial asthma, emphysema, and mitral insufficiency with bronchial catarrh. The treatment was tried on 1 case of whooping cough without any improvement.

Westbrook (*2875*) 1886 obtained good results from the therapy in subacute and chronic bronchitis and claimed some benefit in early cases of tuberculosis. McCaskey (*2867*) 1887 reported 6 months' experience with the pneumatic differentiation treatment on 27 cases. He frankly stated that its use in tuberculosis was justified even if only to increase the comfort of the patients. Histories of cases of pulmonary tuberculosis were also reported by Wood (*2880*) 1887, Curtiss (*2858*) 1887–88, and Pryor (*2872*) 1888. After an experience with 28 cases of tuberculosis, 16 of which were far advanced, Pryor doubted that the method had any value in late stages. There was some relief of cough and other symptoms.

For a similarly cautious attitude toward the use of pneumatic differentiation in pulmonary tuberculosis, the reader is referred to a paper by Abrams (*2852*) 1888. This report contains a description of the Ketchum-Williams cabinet and a discussion of the indications for its use in acute and chronic bronchitis. Abrams believed that little reliance could be placed on reported cases of pulmonary tuberculosis cured by pneumatic differentiation since the diag-

nosis of cases was not corroborated by examination of the sputum for bacilli.

2852. Abrams, A. The pneumatic cabinet and its use in the treatment of pulmonary diseases. *Sacramento med. Times*, 1888, *2:* 407–415. [P, R]

2853. Bowditch, V. Y. The treatment of pulmonary diseases by means of "pneumatic differentiation." *Boston med. Surg. J.*, 1885, *113:* 55–57. [P]

2854. Bowditch, V. Y. The treatment of pulmonary diseases by means of "pneumatic differentiation." *J. Amer. med. Ass.*, 1885, *5:* 124–127. [P, R]

2855. Bowditch, V. Y. Ten months' experience with pneumatic differentiation. *N. Y. med. J.*, 1886, *44:* 370–373; 400–407. [P, Ch]

2856. Bowditch, V. Y. Ten months' experience with pneumatic differentiation. *Trans. Amer. climat. (clin.) Ass.*, 1886, *3:* 47–75. [P, Ch]

2857. Classen, F. L. On the contagiousness of phthisis and the treatment of the disease by pneumatic differentiation. *Albany med. Ann.*, 1886, *7:* 131–140. [P]

2858. Curtiss, R. J. The pneumatic cabinet, with clinical cases. *Peoria med. Mon.*, 1887–88, *8:* 14–17. [Ch]

2859. Donaldson, F., Jr. The pneumatic cabinet and pneumatic differentiation. *Maryland med. J.*, 1885–86, *14:* 297–303. [P]

2860. Fox, S. A. A report of sixty-nine cases of lung disease treated with the pneumatic cabinet. *N. Y. med. J.*, 1886, *43:* 713–717. [P, Ch]

2861. Houghton, A. S. The treatment of pulmonary disease by pneumatic differentiation. *J. Amer. med. Ass.*, 1885, *5:* 506–510. [P]

2862. Jensen, P. C. Acute catarrhal phthitis; recovery. *J. Amer. med. Ass.*, 1885, *5:* 510–512. [P]

2863. Ketchum, J. The theory of the pneumatic cabinet. *N. Y. med. J.*, 1886, *43:* 691–692. [C, P, R]

2864. King, W. H. K. Pneumatic differentiation. *J. Amer. med. Ass.*, 1885, *5:* 670–671. [R]

2865. Martin, H. N. and F. Donaldson. Preliminary account of experiments in regard to the circulatory and respiratory changes observed in animals placed in the pneumatic cabinet. *N. Y. med. J.*, 1886, *43:* 549–550. [P]

2866. Martin, H. N. and F. Donaldson. Preliminary account of experiments in regard to the circulatory and respiratory changes observed in animals placed in the pneumatic cabinet. *Trans. Amer. climat. (clin.) Ass.*, 1886, *3:* 13–16. [P]

2867. McCaskey, G. W. Clinical report of six months' experience with the pneumatic cabinet, with twenty-seven cases. *Boston med. surg. J.*, 1887, *116:* 345–349. [P]

2868. Moeller, [ ]. Un mot sur l'aérothérapie. *J. Méd. Chir. Pharm.*, 1886, *82:* 33–43. [P, R]

2869. Platt, I. H. On the practical application of the pneumatic cabinet. *N. Y. med. J.*, 1886, *43:* 719–721. [P]

2870. Platt, I. H. The physics and physiological action of pneumatic differentiation. *N. Y. med. J.*, 1886, *44:* 515–518; 536–538. [P]

2871. Platt, I. H. The physics and physiological action of pneumatic differentiation. *Trans. Amer. climat. (clin.) Ass.*, 1886, *3:* 76–87. [P]

2872. Pryor, J. H. Results of treatment by the pneumatic cabinet. *Med. Pr. west. N. Y.*, 1888, *3:* 459–466. [P]

2873. Von Ruck, K. Three months' experience with the pneumatic cabinet, with notes and additional cases. *Phys. & Surg., Ann Arbor*, 1886, *8:* 529–543. [P, Ch]

2874. Von Ruck, K. The clinical advantages of the pneumatic cabinet in the treatment of diseases of the respiratory and circulatory organs, with a synopsis of results in ninety-two cases. *Phys. & Surg., Ann Arbor*, 1888, *10:* 291–297. [R]

2875. Westbrook, B. F. Pneumatic differentiation. *N. Y. med. J.*, 1886, *43:* 717–719. [P]

2876. Williams, H. F. Pneumatic differentiation. *Trans. Amer. climat. (clin.) Ass.*, 1885, *2:* 53–64. [C, P]

2877. Williams, H. F. A clinical report of cases treated by pneumatic differentiation. *Trans. Amer. climat. (clin.) Ass.*, 1886, *3:* 17–46. [C, P, Ch]

2878. Williams, H. F. A clinical report of cases treated by pneumatic differentiation. *N. Y. med. J.*, 1886, *44:* 291–295; 318–322; 342–345. [C, P, Ch]

2879. Williams, H. F. Pneumatic differentiation and the pneumatic differential process. Its definition and general suggestions for its application. *J. Amer. med. Ass.*, 1887, *8:* 509–512; 537–541. [C, P]

2880. Wood, W. B. Forced inspiration in pneumatic differentiation. *N. Y. med. J.*, 1887, *45:* 269. [Ch]

IV. PRESSURE BREATHING

In view of the considerable clinical research in the nineteenth century on the therapeutic uses of air under differential pressures, a recent report by Steele on certain aspects of the military and therapeutic significance of pressure breathing may be appropriately reviewed here. In this paper, presented 16 November 1944 at the autumn meeting of the National Academy of Science, Washington, D. C., Steele reviewed studies on the therapeutic application of positive pressure respiration. He drew attention to Barach's observation that asthmatic patients tend to breathe against a resistance made by pursing the lips, a convenient, simple and ready method of application of pressure breathing with increased expiratory pressure. It appears that high degrees of negative pressure in the

alveolar surfaces are harmful and may be responsible for exudation of fluid into the lungs. In patients with emphysema and asthma, breathing against positive pressure may help to clear the lungs of edema. Moreover, blood flow is affected by changes in intrapulmonary pressure, diminished pressure tending to increase cardiac output and increased pulmonary pressure tending to decrease the volume of blood expelled from the heart.

During World War II, pressure breathing has been applied to a use quite different from its therapeutic applications, namely, by increasing the pressure of oxygen in the lungs to increase the ceiling of aviators at very high altitudes. A number of devices have been designed for delivering gases under pressure to the lungs. These devices have been developed to a point where almost any conceivable pattern of pressure breathing may now be available for therapeutic and other uses. Systems have been designed, for example, which will continuously exert a fairly even pressure throughout inspiration and expiration. In most of these continuous pressure arrangements, the expiratory pressure is somewhat higher than the inspiratory. Breathing requires considerable effort and is fatiguing. In intermittent pressure devices, a simple expiratory resistance may be used. Other devices admit intermittent pressure to the lungs during inspiration and these may be used as resuscitators also. Most of these devices require respiration at an imposed rate unless they are manually controlled. Other devices have been arranged to yield various ratios between inspiratory and expiratory pressures.

It appears that pressure breathing serves two principal purposes: (*a*) to decrease pulmonary edema, and (*b*) to decrease anoxia. Positive pressure in the lungs serves anatomically to dilate the bronchioles and the alveoli. Physiologically, according to Steele, it diminishes the effective pressure difference between the blood vessels and the alveoli and so tends to reduce exudation. If pressure breathing is continuous, it moves the region in which the normal tidal air is taken in toward the upper capacity of the lung, or, if intermittent pressure during inspiration is applied, it greatly increases the tidal volume. Pressure breathing also increases slightly the pressure under which gas is delivered to the blood. It tends to decrease the inflow of blood into the right auricle and increases the outflow from the pulmonary vascular bed. This effect on the blood flow in the lungs has been repeatedly referred to by earlier observers who worked on the therapeutic uses of compressed and rarefied air.

Barach has employed respiration against pressure for some time in relief of asthmatic attacks and the pulmonary congestion and edema of heart failure, and there seems little question as to its effectiveness in many patients. Expiratory pressure breathing has also been of value in relieving the pulmonary congestion and edema which tend to follow the surgical relief of the tracheal or bronchial obstruction. Steele raised the question of the possible use of pressure breathing in the treatment of pulmonary edema following irritant gas poisoning. However, since the poison gas produces actual damage within the lungs, this method may be less promising than its use in the pulmonary edema of heart failure.

Pressure breathing equipment has been developed to the point where regulation of the ratio of inspiratory to expiratory pressure is possible and the respiratory rate may be controlled by the patient so that he may breathe as deeply or as rapidly or slowly as he wishes. These developments are seen to be of value in the therapy of cardiac edema, asthma, postoperative atelectasis, hypostatic pneumonia, and edema following relief of tracheal obstruction. Each particular condition may require a distinct pattern of pressure breathing best suited to it. It may be, for example, that expiration against a positive pressure may be too fatiguing for a cardiac patient and that positive pressure during inspiration may be sufficient to clear the lungs of fluid. According to Steele, continuous pressure breathing throughout the whole respiratory cycle may conceivably be more effective in preventing or minimizing edema due to poison gases.

A careful consideration of these developments and the long series of clinical and

experimental investigations on the therapeutic effects of raised atmospheric pressures and of compressed and rarefied air, defective as many of the latter are, permits the hope that further carefully controlled studies in this field may serve to establish certain well-founded indications for treatment by pneumatic methods. The history of the failures of the past should provide a caution against unwarranted optimism but should not discourage further research along promising lines.

V. THERAPEUTIC ACTION OF COMPRESSION AND DECOMPRESSION OF EXTREMITIES AND TRUNK

Not only was the whole body subjected to the action of raised atmospheric pressure as a therapeutic procedure, and not only was the respiration of compressed or rarefied air recommended in the treatment of diseases, but also, partly as a byproduct of these investigations, several investigators experimented with the effects of compression and rarefaction of the arms, legs, or the trunk. It is not within the province of this Sourcebook to discuss the literature dealing with the use of pulsating pressures in peripheral vascular disturbances or other diseases. However, it may be pertinent to call to the reader's attention some of the earliest work on this subject. In 1834, Junod (*2574*) published his first memoir reporting physiological and therapeutic researches on the effects of compression and rarefaction of the air on the whole body as well as upon isolated limbs. His apparatus for compression and rarefaction of the limbs consisted of rigid cylinders into which an arm or leg could be placed. Junod (*2575*) 1835 reported pallor of the skin on compression of the limbs and increase of limb volume and limb temperature and reddening of the skin on reduction of the pressure within the cylinder. After treatment, the limb appeared engorged and the circulation was improved. In addition to these local effects, Junod described certain general systemic effects of local compression and decompression. Junod claimed success for this treatment in paraplegia and other conditions. A discussion of Junod's work was given by Clanny (*2881*) in 1835–36.

The therapeutic use of decompression of the extremities was also recommended by Erpenbeck (*2882*) in 1839. Erpenbeck believed that by drawing blood into the limb and to the surface of the skin, this procedure had a favorable action upon headaches, nosebleed, congestion of the chest, hemoptysis, and asthma.

2881. Clanny, W. R. Researches of M. Junod into the physiological and therapeutic effects of the compression and rarefaction of air on the human body. *Lancet*, 1835–36, *2:* 359–363. [R]

2882. Erpenbeck, H. Die künstliche Luft-Verdünnung als Heil oder Hülfsmittel in mancherlei inneren und äusseren Krankheiten. *Hannoversche Ann. ges. Heilk.*, 1839, *4:* 471–496. [C]

2883. Ford, J. A. The exhausting air treatment of chronic diseases. *Cincinn. Lancet-Clin.*, 1864, N. ser., *7:* 736–738. [P, R]

VI. THERAPEUTIC ACTION OF RAREFIED ATMOSPHERES

While studies were going on, principally in the latter half of the ninteenth century, on the therapeutic action of raised atmospheric pressures, a considerable number of investigations were also being carried out at about the same time on the possible curative action of reduced atmospheric pressures. From the extensive literature in this field, the references included below have been selected as representative. For further studies, the reader should consult Hoff and Fulton (*3*) 1942 and Hoff, Hoff, and Fulton (*4*) 1944.

From very early times, beneficial effects of mountain climates upon persons suffering from pulmonary tuberculosis and other diseases of the chest have been claimed. As early as the seventeenth century, Henshaw (see Simpson (*2609*) 1857) believed that the curative action of mountain climate might lie in the lower atmospheric pressures prevailing at altitudes and this was the theory upon which he proposed the construction of a chamber in which the atmosphere could be rarefied or compressed. In 1862, Jourdanet (*2897*) also proposed using artificially reduced atmospheric pressures for therapeutic purposes.

The reader may consult a thesis published in 1877 by Schyrmunski (*2902*) who discussed

the therapeutic effect of pneumatic cabinets in which patients were subjected to a reduction in pressure of 3/7 atmosphere.

There is a vast literature upon the effects of high altitudes upon pulmonary tuberculosis which will not be referred to. Reference may be made, however, to a report on the influence of decompression upon the course of experimental tuberculosis in guinea pigs by Del Rio (*2893*) 1928.

The problem of the management of pulmonary tuberculosis by treatments in decompression chambers and the use of decompression chambers in the prophylaxis and therapy of various other diseases of the respiratory tract were also discussed by Danielski (*2890*) 1934. Reference may also be made to therapeutic use of oxygen-poor air by Schmidt and David (*2901*) 1911 and Charlet (*2888*) 1931. In 1941, Andrews, Roth, and Ivy (*2884*) published a preliminary report on the use of reduced atmospheric pressure in the treatment of paranasal sinusitus.

An unusual development in high altitude therapy has been the treatment of whooping cough by high altitude flights. This treatment has been reviewed by the following workers: Kettner (*2898*) 1927, Nagel (*2900*) 1935, Bober (*2885*) 1939, Chaminaud (*2887*) 1940, and Delgado Correa (*2892*) 1940. Attention should be called to a paper by Clamann and Becker-Freyseng (*2889*) which appeared in 1940 on the treatment of whooping cough not only by altitude flights but also by runs in the decompression chamber.

It has been observed that Graves' disease shows symptomatic improvement at high altitudes and the following authors may be consulted for references to the treatment of hyperthyroidism by high altitude or decompression therapy: Lax (*2899*) 1928, Hecht (*2896*) 1928, and Guhr (*2895*) 1932. It is of some interest that hyperthyroidic individuals are less tolerant of high altitudes than normal subjects while patients with hypothyroidism appear to have an increased tolerance. This difference in tolerance is doubtless associated with characteristic differences in metabolic rate and hence oxygen requirements of these individuals.

A number of reports dealing with the effects of changes in pressure upon the growth of cells have appeared. Some of these are discussed on page 187. The reader may also consult a paper by Sundstroem and Giragossintz (*2905*) 1929–30 on the curability of malignancy in rats by a low pressure environment.

Several studies have been initiated on the effects of anoxic shock as a possible method of treatment for schizophrenia. Two reports dealing with this problem have been given by Green and Adriani (*2894*) 1940 and Tannenberg (*2907*) 1940.

2884. Andrews, A. H., L. W. Roth, and A. C. Ivy. On the use of reduced atmospheric pressure in the treatment of paranasal sinusitis. A preliminary report. *Quart. Bull. Nthwest. Univ.*, (b), 1941, *15:* 46–52. [P]

2885. Bober, S. Leczenie krztuśca lotami wysokośćiowymi. (The treatment of pertussis by altitudinal flights.) *Polsk. Przegl. Med. Lotn.*, 1939, *8:* 48–55. (With French and English summaries.)

2886.*Broekema, H. [High altitude flights in therapy of whooping cough.] *Maandschr. Kindergeneesk.*, 1939, *8:* 479–490. (With English summary.) [P]

2887. Chaminaud, C. G. Coqueluche y aviación. *Sem. méd., B. Aires*, 1940, *47*(2): 832–836. [P]

2888. Charlet, R. Le vol en avion dans les cures thérapeutiques d'air pur et d'altitude. *Pr. méd.*, 1931, *39:* 1036–1037. [P]

2889. Clamann, H. G. and H. Becker-Freyseng. Über Erfahrungen mit Keuchhusten-Höhenflügen und Unterdruckkammer-Behandlungen. *Dtsch. med. Wschr.*, 1940, *66:* 61–65. [P]

2890. Danielski, Z. Komory pneumatyczne w profilaktyce i lecznictwie chorób płuc i dróg oddechowych. [Pneumatic chambers in prophylaxis and therapy of diseases of respiratory tract and of lungs.] *Polsk. Gaz. lek.*, 1934, *13:* 612–615. [P]

2891. David, O. Die therapeutische Verwertung sauerstoffarmer Luft bei Anämien. *Dtsch. Arch. klin. Med.*, 1913, *109:* 129–150. [P]

2892. Delgado Correa, B. Tratamiento de la tos convulsa por vuelos de altura en avión. *Arch. Pediat. Uruguay*, 1940, *11:* 915–920. [P]

2893. Del Rio, S. Über den Einfluss der Luftverdünning auf den Ablauf der experimentellen Meerschweinchentuberkulose. *Beitr. Klin. Tuberk.*, 1928, *69:* 636–640. [P]

2894. Green, W. F. and J. Adriani. Effects of anoxia induced by nitrogen inhalation in treatment of psychoses. *Arch. Neurol. Psychiat., Chicago*, 1940, *44:* 1022–1030. [P]

2895. Guhr, M. Blutdruck und Pulszahl Thyreotoxiker während und nach dem Aufenthalt in der Höhenluft. *Verh. dtsch. Ges. inn. Med.*, 1932, *44:* 496–502. [P]

2896. Hecht, V. Zur Pathologie und Therapie der Basedowschen Krankheit und der Hyperthyreosen im Höhenklima. *Wien. klin. Wschr.*, 1928, *41:* 1154–1157; 1195–1199. [P]

2897. Jourdanet, D. *L'air rarefie dans ses rapports avec l'homme sain et avec l'homme malade.* Paris, J.-B. Baillière et fils, 1862, 80 pp. [P, R]

2898. Kettner, A. H. Keuchhustentherapie im Flugzeug. *Med. Welt*, 1927, *1:* 1599. [P]

2899. Lax, H. Unterdruckbehandlung bei Morbus Basedowii. *Verh. dtsch. Ges. inn. Med.*, 1928, *40:* 263–268. [P]

2900. Nagel, H. G. Beitrag zur Frage der Klimatotherapie des Keuchhustens durch Flugzeugreisen *Fortschr. Med.*, 1935, *53:* 529–531. [P, R]

2901. Schmidt, A. and O. David. Ueber die therapeutische Verwendung sauerstoffarmer Luft beim Menschen. *Münch. med. Wschr.*, 1911, *58:* 939–942. [P]

2902. Schyrmunski, Mendel. *Ueber den Einfluss der verdünnten Luft auf den menschlichen Organismus.* Inaug.-Diss. (Med.) Berlin, Gustav Schade, 1877, 32 pp. [P, R]

2903. Singer, W. Über den Einfluss der Luftdruckerniedrigung auf den Verlauf der Tuberkulose. *Beitr. Klin. Tuberk.*, 1928–29, *71:* 572–575.]P[

2904. Singer, W. Beitrag zum Problem der Tuberkulosebehandlung in der Unterdruckkammer. *Klin. Wschr.*, 1929, *8:* 785–787. [P]

2905. Sundstroem, E. S. and G. Giragossintz. A demonstration of the curability of malignancy in rats by a low pressure environment. *Proc. Soc. exp. Biol., N. Y.*, 1929–30, *27:* 511–514. [P]

2906.* Tammann, H. and O. Bruns. Spirometrische Untersuchungen an Bergarbeitern. Ein Beitrag zur Genese des Emphsems. *Z. ges. exp. Med.*, 1923, *33:* 350–367. [P]

2907. Tannenberg, J. Advantages and danger of combined anoxic and insulin shock. Report of animal experiments with a possible method of treatment for schizophrenia. *Arch. Neurol. Psychiat., Chicago*, 1940, *44:* 811–828. [P]

2908. Anon. The therapeutic value of flying. *Flying, N. Y.*, 1921, *10:* 132; 146; 154. [P]

VII. CLIMATIC THERAPY

Inhalation of air, especially heated or cooled air medicated with various vapors, has long been recommended and used for curative purposes. Of the large body of literature on this subject, only a few references are given. In 1879, von Kaczorowski (*2914*) recommended the use of cold air as an antipyretic and antiseptic. Climatic therapy was also recommended by Speck (*2916*) in 1883. An apparatus for delivering medicated vapors and oxygen for therapeutic purposes was described in 1887 by Dujardin-Beaumetz (*2913*). This is but one of a great number of such apparatuses that have been described and used. The reader may consult a paper by Cervello (*2912*) published in 1889 on the value of inhalation of hot air in tuberculosis. A discussion of aerotherapy was also given in 1895 by Lagrange (*2915*).

For a modern consideration of the possibilities of aerotherapy, reference may be made to two papers published in 1943 by Bory (*2910, 2911*). This author proposed specially constructed chambers or climatic rooms in hospitals in which the humidity, temperature, and pressure could be controlled. It was proposed that the air delivered to such a climatic chamber could be filtered and so rendered free of dust and germs. Special medications could be introduced as required in gaseous or vapor form. Bory believed that various respiratory diseases such as tuberculosis might be amenable to this form of treatment. He proposed, for instance, the treatment of syphilis by inhalation of mercurial vapors and psoriasis by subjecting the patient to an atmosphere charged with sulfur dust. He also considered the possibility of using such a room for the continued administration of oxygen and certain sedatives by inhalation.

Conditions of life within the confined spaces of submarine compartments offer an opportunity for controlled investigations of the effects on health of various conditions of temperature, humidity, atmospheric pressure, and bacterial and dust content of the air, and whereas so-called climatic therapy may have very limited military application, nevertheless the regulation of the environment does play a vital role in the maintenance of health. Studies of optimum conditions of habitability should be conducted in laboratories adequately staffed and equipped for this purpose as well as in naval vessels specifically assigned to research.

2909. Berg, E. Mittheilungen über Stickstoffinhalationen bei Lungenkrankheiten nach Dr. G. Trentler. *St Petersb. med. Wschr.* (*Z*), 1881, *6:* 303–305.

2910. Bory, L. Sur l'emploi des gaz, poussières et vapeurs en thérapeutique. L'atmothérapie. *C. R. Acad. Sci., Paris*, 1943, *217:* 410–412.

2911. Bory, G. De la possibilité de réaliser par des méthodes industrielles une thérapeutique par les gaz: l'aérogazo-thérapie. *C. R. Acad. Sci., Paris*, 1943, *217:* 464–466.

2912. Cervello, V. Inalazioni di aria calda coll-'apparecchio del Weigert. *Sicilia med.*, 1889, *1:* 833–839.

2913. Dujardin-Beaumetz, [ ]. Sur l'atmiomètre du professeur Jacobelli (de Naples). *Bull. Acad. Méd. Paris*, 1887, Sér. 2, *18:* 177–184.

2914. Kaczorowski, [ ] von. Die kalte Luft als Antipyreticum und Antisepticum. *Dtsch. med. Wschr.* 1879, *5:* 15–17; 25–29; 37–41; 49–54.

2915. Lagrange, F. L'installation d'une cure d'air. *Rev. Hyg. thér.*, 1895, *7:* 268–285.

2916. Speck, [ ]. Ueber Luftcuren. *Arch. exp. Path. Pharmak.*, 1883, *17:* 278–290.

VIII. CLIMATOLOGY

It has been repeatedly claimed that meteorological conditions affect human health. Slack (*2929*), for example, noted in 1826 that climatic change in barometric pressure was associated with variations in the incidence of colds and other diseases. Other effects on bodily economy related to barometric pressure changes were noted by Kupfer (*2922*) in 1827. The effect of humidity of the air upon the functions of the human body were reviewed in 1832 by Stohlmann (*2931*).

The influence of the humidity of the atmosphere on health was discussed in 1855 by Hunt (*2920*). In 1869, Hewson (*2919*) reported figures indicating that temperature and humidity have little to do with over-all fatalities in acute surgical operations. The reader may also consult a paper by Williamson (*2932*) 1876 on the supposed relation between hemorrhage and altered barometric pressure with observations on 120 cases of hemoptysis. Löwenfeld (*2923*) 1896 considered that various neurotic manifestations may be produced or exacerbated by meteorological causes. During World War II, medical officers, stationed in areas where cold, damp, foggy weather prevails, have made similar observations.

In 1920, Apolant (*2917*) published a report on the effect of weather on disease incidence. In an analysis of the vital statistics and weather reports of Chicago for the period between January 1934 and April 1926, Bundesen and Falk (*2918*) reported in 1926 that the mortality rates from organic heart disease, cerebral hemorrhage, and chronic nephritis were unusually high during the periods of low temperature and high when the temperature was low. There was no uniform correlation between the fluctuations in mortality from these specified causes of death and meteorological variations in the barometric pressure.

Other reports on climatology by Loewy (*2924*) 1931, Spillmann (*2930*) 1931, and Perlewitz (*2926*) 1936 may be consulted. The standard reference on medical climatology is Peterson's four-volume work (*2927*) published between 1934 and 1937. For a more popular treatment of the subject, the reader may refer to the book by Mills (*2925*) 1942.

The field of climatology does not strictly come within the province of submarine medicine. However, submarine personnel are subjected to artificial environments for prolonged periods. Moreover, indications point to even greater periods of submergence and wider ranges of operation in future submarine activities. It therefore becomes a matter of importance to secure accurate information upon the optimal environmental conditions for the maintenance of health and efficiency of submarine crews. Research work designed to obtain such accurate knowledge should therefore receive support.

2917. Apolant, [ ]. Ueber Beziehungen des Barometerdruckes zu Krankheiten. *Dtsch. med. Wschr.*, 1920, *46:* 1256.

2918. Bundesen, H. N. and I. S. Falk. Low temperature, high barometer and sudden death. *J. Amer. med. Ass.*, 1926, *87:* 1987–1989.

2919. Hewson, A. On the influence of the weather over the results of surgical operations, and on the value of the barometer as a guide in the choice of the time for and the prognosis in such operations, as shown by the results of "immediate amputations" during a period of thirty years in the Pennsylvania Hospital. *Penn. Hosp. Rep.*, 1869, *2:* 2–35.

2920. Hunt, S. B. The report of the committee on the hygrometrical state of the atmosphere in various localities, and its influence on health. *Trans. Amer. med. Ass.*, 1855, *8:* 327–346.

2921. Kestner, O. Die physiologischen Wirkungen des Klimas. *Bethes Handb. norm. path. Physiol.*, 1926, *17*, Correlationen 3*:* 498–559.

2922. Kupfer, Heinrich Edward. *De vi, quam aër pondere suo et in motum sanguinis, et in absorptionem exercet.* Thesis (Med.) Leipzig, Hirschfeld, 1827, iv, 68 pp.

2923. Löwenfeld, L. Ueber "Witterungsneurosen." *Münch. med. Wschr.*, 1896, *43:* 93–96.

2924. Loewy, A. Ueber Klimatophysiologie. *Dtsch. med. Wschr.*, 1931, *57:* 789–790; 852–855; 893–896; 978–981; 1022–1026; 1112–1114; 1157–1159; 1200–1202.

2925. Mills, Clarence A. *Climate makes the man.* New York, Harper & Brothers, 1942, vi, 320 pp. [R]

2926. Perlewitz, P. Die Klimastockwerke in der Atmosphäre. *Ann. Hydrogr., Berl.*, 1936, *64:* 206–209.

2927. Peterson, William F. *The patient and the weather.* Ann Arbor, Mich., Edwards Brothers, Inc., 1934–37, 4 vols. [R]

2928. Poznanski, [ ]. Note sur quelques effets des vicissitudes de la pression atmosphérique. *C. R. Acad. Sci., Paris*, 1857, *44:* 1158–1159.

2929. Slack, D. B. Remarks upon the characteristic effects of the variations of atmospheric pressure upon the human system. *New Engl. J. Med. Surg.*, 1826, *15:* 371–379.

2930. Spillmann, L. Réaction de l'organisme humain aux variations de la pression barométrique. *Rev. méd. Est.*, 1931, *59:* 717–722.

2931. Stohlmann, Friedrich Wilhelm. De aëris *humidi in corpus humanum effectu.* Thesis (Med.) Berlin, Nietacke, 1832, 48 pp.

2932. Williamson, J. M. On the supposed relation between haemorrhage and altered barometric pressure, with observations on 120 cases of haemoptysis. *Lancet*, 1876, *2:* 321–322.

Human Factors in Design and Operation of Submarine Instruments and Controls; Submarine Illumination

The duties of submarine personnel involve the reading of instruments and operation of various types of controls. It is essential that these instruments and controls be designed, located, and illuminated so that they can be used with maximum efficiency. Human factors in engineering design are being investigated in many military and industrial fields. In particular, research programs are underway which have as their objective the design and placement of aircraft instruments and controls so as to insure efficient performance, to minimize errors, and to reduce accident rates. A survey of the scattered literature on the subject of anatomical, physiological, and psychological factors in engineering design has revealed that it is difficult to discover general biological principles which may be set forth in the form of simple rules to guide engineers. However, progress is being made and the selected references listed here may serve as an aid to readers interested in the subject as it applies to submarines. A complete bibliography is shortly to be issued by the Bureau of Medicine and Surgery of the U. S. Navy and readers having access to classified material should consult this volume.

To protect dark adaptation, it is necessary that red illumination be used at night in all compartments of the submarine except the engine rooms and the maneuvering room. Red lighting, however, creates certain psychological problems, for example, in the preparation and serving of food which takes on strange and sometimes unpleasant colors in red light.

Submarine illumination is artificial at all times and the selection and placement of lights is an important consideration. Because of the lack of clear overhead and bulkhead space, the installation of lights in optimal positions is sometimes difficult. Fluorescent light appears preferable to incandescent lighting. However, shock-proof fluorescent lamps have not yet been developed and for this reason, incandescent lamps are used on war patrols.

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2939. Hecht, S. and E. U. Mintz. The visibility of single lines at various illuminations and the retinal basis of visual resolution. *J. gen. Physiol.*, 1939, *22*(5): 593–612.

2940. Luckiesh, Matthew. *Light, vision and seeing.* New York, D. Van Nostrand Co., Inc., 1944, xiv, 323 pp.

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2942. Moon, P. and D. E. Spencer. The visual effect of non-uniform surrounds. *J. opt. Soc. Amer.*, 1945, *35:* 233–248.

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Medicolegal Aspects of Compressed Air Work

A careful search of the legal literature reveals relatively few court decisions involving caisson disease. The legal cases cited below indicate the attitude taken by the courts in relation to compensation claims for injuries received while engaged in caisson work or for disabilities associated with caisson disease.

In the case of the *Missouri Valley Bridge and Iron Co.* vs. *Ballard* (*2956*) 1909, the plaintiff was a sand-hog engaged in building piles for a bridge for the Southern Kansas Railway Co., the construction being carried out under the Missouri Valley Bridge and Iron Co. No details were given in the record of the pressure, duration of shift, time interval between "locking out," and the onset or the severity of the disease. The court ruled that the Southern Kansas Railway Co. was not responsible for any cases of caisson disease contracted by workmen since this illness was inherent in caisson work. It was held that the employer is not responsible if the employee knows the dangers inherent in the type of work in question.

The case of *Williams* vs. the *Missouri Valley Bridge and Iron Co.* (*2958*) 1920 concerned a fatal accident to a caisson worker on the construction of a bridge over the River Rouge by the Missouri Valley Bridge and Iron Co. in 1919. The caisson at the time of the accident was 70 to 80 ft. below the surface of the water and the air pressure in the working chamber was 37 to 40 lb. per sq. in. (gauge). The workers climbed a ladder to the top of the caisson where they entered the lock. The pressure in the lock was usually reduced at a rate of 1 lb. per minute. On 4 July 1919, Williams (the worker in question) and his companions entered the lock, Williams standing on the ladder. A fellow worker in charge of the valve released the pressure in the lock too rapidly. Williams was suddenly affected by the decompression and fell off the ladder, striking his chest on the head of the man below him and his head on the side of the lock. He was given medical aid but died within a few hours. The defendants argued that the fall was caused by conditions peculiar to the industry in which the man was engaged and that death was not actually due to accidental causes. The court ruled that the cause of death was not inherent but was brought on by the inattention and neglect of a co-employee (releasing the air too rapidly). Therefore, the accident arose directly from employment. It was also ruled that the defendant did not suffer from a true occupational disease since there was no slow development of the condition. The case was awarded to the plaintiff (Williams' widow) in accordance with a prior decision of the Industrial Accident Board.

The case of *Beaty et al.* vs. the *Foundation Co. et al.* (*2953*) 1928 concerned a worker engaged in preparing footings for the Union Trust Building in Detroit in 1927. No details were given in the record of the pressure under which work was being carried out. At 4 o'clock in the morning of 2 September 1927, the deceased "locked out" and went home. Shortly thereafter, he vomited and lost the use of the legs. There was also total blindness. The patient died at 1:30 on the same afternoon. Death was ascribed to "bends" due to too rapid release of pressure during the period of "locking out." The court held that death from "bends" would not of itself make the company responsible since "bends" is an occupational resultant and does not *per se*

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authorize compensation. However, when caused by a "fixed and single fortuitous and preventable circumstance," "bends" is not an occupational disease but an accident as covered by the Workmen's Compensation Law. It was found by the Department of Labor Investigating Board that while the pressure should have been released at a rate of 1½ lb. per minute, it was actually released at twice this speed. The fact that fellow workmen suffered no ill effects or that the deceased had had previous attacks of caisson disease was held immaterial. Since too sudden decompression caused the illness in question, and since there was no willful or intentional misconduct on the part of the deceased, death was held to be due to compensable accident and the decision of award to the plaintiff was upheld.

In the case of *Taylor* vs. *The List and Weatherby Construction Co.* (*2957*) 1933, the plaintiff was engaged in work on the construction of a bridge across the Red River at Shreveport, La. Work was carried out at a depth of 75 ft. below the surface of the water. According to the company rules, workers were limited to 3-hour shifts. After "locking out" they were required to report at the "hog house" for a hot shower, hot coffee, and 1 hour's rest. The plaintiff was stricken with symptoms of the "bends" while taking a shower following a 3-hour shift. He was taken immediately to a recompression chamber where he was kept at pressure for 1 hour. Recompression gave no relief, however. The patient was treated for 8 weeks by the company physician and was then discharged. He continued to treat himself with hot applications. The plaintiff complained that he had not worked since the time of the accident. He stated that he had severe pains in the shoulder and could not raise the arm above horizontal without great pain. Two doctors who had examined the plaintiff stated that they believed he was still suffering from "bends" pain. The company physician testified that in his view the plaintiff was cured but he was unwilling to deny that he suffered from the pains complained of. The court accepted the medical opinion indicating that the plaintiff was still suffering from pain and therefore upheld a lower court decision in which judgment had been given for the plaintiff.

On 25 February 1929 a diver, Gerlaske, spent 45 minutes in deep water working on piling. When drawn to the surface, he was found to be suffering from shock and cold. The patient died after a lingering illness of approximately 2 months. After his death, the patient's widow filed a statement and claim against the Maryland Casualty Co. The Compensation Board claimed that death was due, not to an industrial accident, but to natural causes complicated by an unrelated disease. The court found no evidence that the case was not one of industrial accident and judgment in favor of the defendant was upheld. (See *Maryland Casualty Co.* vs. *Gerlaske et al.* (*2955*) 1934.)

A legal case of interest in connection with work under high pressure is that of *Howell* vs. the *St. Clair Coal Co.* (*2954*) 1930. The plaintiff claimed compensation for the accidental death of her husband while at work in a mine of the St. Clair Coal Co. The deceased was a man 49 years of age, in good health except for evidences of arteriosclerosis. While drilling a hole in a chute on 12 March 1926, he fell unconscious and died 3½ hours later. The chute, which opened into a gangway, was ventilated by compressed air blown in at a pressure of 60 lb. per sq. in. Death was stated to be due to "over-exertion caused by drilling resulting in cerebral apoplexy." The doctor called as a witness expressed his opinion that the combined effect of work in compressed air and undue exertion caused the apoplexy. However, the court correctly found that the use of compressed air in ventilating the chute did not necessarily raise the barometric pressure in the chute and therefore that the lower court had been justified in setting aside the award to the plaintiff.

Foı further reports on the medicolegal aspects of work in compressed air, the reader may refer to papers by the following authors: Lecaplain (*2949*) 1906, Cardon (*2947*) 1908, Langlois (*2948*) 1910, Silberstern (*2951*) 1910, Pettazzi (*2950*) 1915, and Boycott (*2946*) 1935. Reports dealing with regulations govern-

ing working conditions in caissons and underwater tunnel construction projects may be found on page 267.

2946. Boycott, G. W. M. Prevention of compressed air illness. Obsolete statutory regulations as an obstacle to progress. *J. Hyg., Camb.*, 1935, *35*: 318–321.

2947. Cardon, G. Contributo allo studio medicolegale della malattie da lavoro in aria compressa. *Ramazzini*, 1908, *2:* 362–373.

2948. Langlois, J.-P. La réglementation du travail. *Pr. méd.*, 1910, *18:* 681-682.

2949. Lecaplain, J. *Suites médicales tardives des affaires judiciaires relatives à l'hystéro-traumatisme.* Thèse (Méd.) Paris, Imprimerie des Facultés A. Michalon, 1906, 149 pp.

2950. Pettazzi, A. Osservazioni cliniche e considerazioni medico-legali sulla patologia del lavoro in aria compressa. *Ramazzini*, 1915, *9:* 118–152.

2951. Silberstern, P. Gesetzlicher Arbeiterschutz bei Caissonarbeiten in Frankreich. *Amtsarzt.*, 1910, *2:* 21–23

2952. Anon. Caisson disease. *Lancet*, 1905, *1:* 1173.

2952a. Anon. The proposed Swiss regulations for the prevention of accidents among caisson workers and the German ordinance of 28. VI. 1920 for the protection of workers in compressed air. Abstr: *J. industr. Hyg.*, 1933, *15:* 83–84.

2953. Beaty et al. *vs.* Foundation Co. et al. 245 Mich. 256, 222 N.W. 77 (1928).

2954. Howell *vs.* St. Clair Coal Co. 95 Pa. Super 310 (1930).

2955. Maryland Casualty Co. *vs.* Gerlaske et al. 68 F. (2d) 497 (1934).

2956. Missouri Valley Bridge and Iron Co. et al. *vs.* Ballard. 53 Tex. Civ. App. 110, 116 S.W. 93 (1909).

2957. Taylor *vs.* List and Weatherby Construction Co. (La.). 146 So. 353 (1933).

2958. Williams *vs.* Missouri Bridge and Iron Co. 212 Mich. 150, 180 N.W. 357 (1920).

Key to Abbreviations of Journals and Handbooks Cited

Abbreviations not included in *A World List of Scientific Periodicals Published in the Years* 1900-1933, *2nd Ed.*, London, 1934, are marked with an asterisk

Accad. med. Accademia medica. Genova.

*Acta aerophysiol.** Acta aerophysiologica. Hamburg.

Acta brev. neerl. Physiol. Acta brevia Neerlandica de physiologia, Pharmacologia, Microbiologia, e.a. Amsterdam.

Acta chir. scand. Acta chirurgica Scandinavica. Stockholm.

Acta med. scand. Acta medica Scandinavica. Stockholm.

Acta ophthal., Kbh. Acta ophthalmologica. Kjøbenhavn.

Acta oto-laryng., Stockh. Acta oto-laryngologica. Stockholm.

Acta Soc. ophthal. jap. Acta Societatis ophthalmologicae Japonicae. Ganka Kenkyû-Kwai. Tokyo.

*Ärzt. IntelligBl.** Aerztliches Intelligenz-Blatt. München.

*Ärztl. CentAnz.** Aerztlicher Central Anzeiger, Wien.

Ärztl. Rdsch. Ärztliche Rundschau. München.

Ärztl. SachverstZtg. Aerztliche Sachverständigen-Zeitung. Berlin.

Ärztl. ZentAnz. Ärztlicher-Zentralanzeiger. Hamburg.

Air Serv. Inform. Circ. Air Service Information Circular. Washington.

Albany med. Ann. Albany Medical Annals. Albany.

Allg. med. ZentZtg. Allgemeine medizinische Zentralzeitung. Berlin.

Allg. wien. med. Ztg. Allgemeine Wiener medizinische Zeitung. Wien.

Amer. Heart J. American Heart Journal. St. Louis.

Amer. J. Bot. American Journal of Botany. Lancaster.

Amer. J. Cancer. American Journal of Cancer. New York.

Amer. J. Hyg. American Journal of Hygiene. Baltimore.

*Amer. J. med. Jurisprud.** American Journal of Medical Jurisprudence. Boston.

Amer. J. med. Sci. American Journal of the Medical Sciences. Philadelphia.

Amer. J. Obstet. Gynec. American Journal of Obstetrics and Gynecology. St. Louis.

Amer. J. Ophthal. American Journal of Ophthalmology. Cincinnati.

Amer. J. Physiol. American Journal of Physiology. Baltimore.

Amer. J. Psychiat. American Journal of Psychiatry. New York.

Amer. J. Psychol. American Journal of Psychology. Ithaca.

Amer. J. publ. Hlth. American Journal of Public Health. Albany.

Amer. J. Roentgenol. American Journal of Roentgenology. Springfield, Ill.

Amer. J. Surg. American Journal of Surgery. New York.

Amer. J. trop. Dis. American Journal of Tropical Diseases and Preventive Medicine. Official Organ of The American Society of Tropical Medicine. New Orleans.

*Amer. Labor Legisl. Rev.** American Labor Legislation Review. New York.

Amer. Med. American Medicine. Philadelphia.

Amer. Rev. Tuberc. American Review of Tuberculosis. New York.

Amtsarzt. Der Amtsarzt. Zeitschrift für öffentliches Gesundheitswesen. Leipzig.

Anesth. & Analges. Anesthesia and Analgesia. New York.

*Anesth. & Analgés., Paris.** Anesthésie et Analgésie. Paris.

*Anesthesiol.** Anesthesiology. Journal of the American Society of Anesthetists, Inc. New York.

*Ann. Allergy.** Annals of Allergy. St. Paul, Minn.

Ann. Chim. (Phys.). Annales de Chimie (et de Physique). Paris.

Ann. clin. Med. Annals of Clinical Medicine. Baltimore.

Ann. Hydrogr., Berl. Annalen der Hydrographie und maritimen Meteorologie. (Deutsche Seewarte.) Berlin.

Ann. Hyg. publ., Paris. Annales d'hygiène publique et de médecine légale (industrielle et sociale). Paris.

Ann. Igiene (sper.). Annali d'igiene (sperimentale). Torino.
Ann. intern. Med. Annals of Internal Medicine. Lancaster, Pa.
Ann. Mal. Oreil. Larynx. Annales des maladies de l'oreille, du larynx. Paris.
Ann. Méd. lég. Annales de médecine légale. Paris.
Ann. Med. nav. colon. Annali di medicina navale e coloniale. Roma.
Ann. Min., Paris. Annales des mines. Paris.
Ann. Oculist., Paris. Annales d'oculistique. Paris.
Ann. Oto-laryng. Annales d'oto-laryngologie. Paris.
Ann. Otol., etc., St. Louis. Annals of Otology, Rhinology and Laryngology. St. Louis.
Ann. Phys., Lpz. Annalen der Physik. Leipzig.
Ann. Ponts Chauss. Annales des ponts et chaussées. Paris.
Ann. Soc. méd.-chir. Liége. Annales de la Société médico-chirurgicale de Liége.
Ann. Soc. Sci. méd. nat. Brux. Annales (et Bulletin). Société royale des sciences médicales et naturelles de Bruxelles.
Ann. Surg. Annals of Surgery. Philadelphia.
*Annu. Rev. Physiol.** Annual Review of Physiology. Stanford University P. O., Cal.
Apothekerztg. Berl. Apotheker-Zeitung. Berlin.
*Arbeit und Gesundh.** Arbeit und Gesundheit. Berlin.
*Arbeiterschutz.** Arbeiterschutz. Unfallverhutüng. Gewerbehygiene. Berlin.
Arbeitsphysiologie. Arbeitsphysiologie. Berlin.
Arch. Anat. Physiol., Lpz. Archiv für Anatomie und Physiologie. Leipzig.
Arch. Anthrop. crim. Archives d'anthropologie criminelle, de médecine légale et de psychologie normale et pathologique. Lyon.
Arch. Antrop. crim. Archivio di antropologia criminale, psichiatria e medicina legale. Milano.
Arch. Augenheilk. Archiv für Augenheilkunde. München.
Arch. brasil. Med. Archivos brasileiros de medicina. Rio de Janeiro.
Arch. Cardiol. Hematol., Madr. Archivos de cardiología y hematología. Madrid.
Arch. Élect. méd. Archives d'électricité médicale, etc. Paris.
Arch. exp. Path. Pharmak. Naunyn-Schmiedebergs Archiv für experimentelle Pathologie und Pharmakologie. Berlin.
Arch. Fisiol. Archivio di fisiologia. Firenze.
Arch. gén. Méd. Archives Générales de Médicine. Paris.
Arch. Gewerbepath. Gewerbehyg. Archiv für Gewerbepathologie und Gewerbehygiene. Berlin.
Arch. Hyg., Berl. Archiv für Hygiene (und Bakteriologie). Berlin; München.
Arch. int. Laryng. Archives internationales de laryngologie, d'otologie et de rhinologie. Paris.
Arch. int. Pharmacodyn. Archives internationales de pharmacodynamie (et de thérapie). Liége.
Arch. intern. Med. Archives of Internal Medicine. Chicago.
Arch. ital. Biol. Archives italiennes de biologie. Pise.
Arch. ital. Otol. Archivio italiano di otologia, rinologia e laringologia. Como.
Arch. méd. belges. Archives médicales belges. Liége.
*Arch. med. ferroc.** Archivos medicos ferrocarrileros. México. D.F.
Arch. Méd. Pharm. milit. Archives de médecine et de pharmacie militaires. Paris.
Arch. Méd. Pharm. nav. Archives de médecine et de pharmacie navales. Paris.
Arch. Neurol., Paris. Archives de neurologie. Paris.
Arch. Neurol. Psychiat., Chicago. Archives of Neurology and Psychiatry. Chicago.
Arch. Ohr.-, Nas.-, u. KehlkHeilk. Archiv für Ohren-, Nasen- und Kehlkopfheilkunde. Berlin.
*Arch. Ophthal., Chicago.** Archives of Ophthalmology. Chicago.
Arch. Ophthal., N. Y. Archives of Ophthalmology. New York.
Arch. Orthop. MechTher. Archiv für Orthopädie, Mechanotherapie und Unfallchirurgie. Berlin.
Arch. Otol., N. Y. Archives of Otology. New York.
Arch. Otolaryng., Chicago. Archives of Otolaryngology. Chicago.
*Arch. Path., Chicago.** Archives of Pathology. Chicago.
Arch. Pediat. Archives of Pediatrics. New York.
Arch. Pediat. Uruguay. Archivos de pediatría del Uruguay. Montevideo.
Arch. phys. Ther. Archives of Physical Therapy. Chicago.
*Arch. Physiol. norm. path.** Archives de physiologie normale et pathologique. Paris.
Arch. Psychiat. Nervenkr. Archiv für Psychiatrie und Nervenkrankheiten. Berlin.
Arch. Psychol. N. Y. Archives of Psychology. New York.
Arch. Schiffs- u. Tropenhyg. Archiv für Schiffsund Tropenhygiene, unter besonderer Berrücksichtigung der Pathologie und Therapie. Leipzig.
Arch. Sci. med. Archivo per le scienze mediche. Torino
Arch. Surg., Chicago. Archives of Surgery. Chicago.
Army med. Bull. Army Medical Bulletin. Carlisle, Pa.
Art méd., Anvers. L'art Médical. Anvers.
*Ass. med. J.** Association Medical Journal. London.
Ateneo parmense. Ateneo Parmense. A cura della reale Università e della Società di medicina e scienze naturali di Parma.
Atti Accad. Torino. Atti della R. Accademia delle scienze. Torino.
*Atti Congr. int. Med. Farm. milit.** Atti del Congresso internazionale di medicina e farmacia militare. Roma.
Aust. J. exp. Biol. med. Sci. Australian Journal of Experimental Biology and Medical Science. Adelaide.
Aust. med. Gaz. Australasian Medical Gazette. Sydney.

Beitr. klin. Chir. Beiträge zur klinischen Chirurgie. (Bruns Beiträge.) Berlin.

Beitr. Klin. Tuberk. Beiträge zur Klinik der Tuberkulose und spezifischen Tuberkuloseforschung. (Klinische Beiträge.) Berlin.

Beitr. path. Anat. Beiträge zur pathologischen Anatomie und zur allgemeinen Pathologie. Jena.

Berl. klin. Wschr. Berliner klinische Wochenschrift. Berlin.

*Bethes Handb. norm. path. Physiol.**Handbuch der normalen und pathologischen Physiologie. Herausgegeben von A. Bethe. Berlin, Julius Springer.

Bezopas. Truda Gorn. Prom.

Bgham med. Rev. Birmingham Medical Review. London.

Bibl. Éc. haut. Étud. Bibliothèque de l'École des hautes études. Section des sciences naturelles. Paris.

Biochem. Bull. Biochemical Bulletin. Lancaster, Pa.

Biochem. J. Biochemical Journal. London.

Biochem. Z. Biochemische Zeitschrift. Berlin.

Biol. Bull. Wood's Hole. Biological Bulletin of the Marine Biological Laboratory, Wood's Hole, Mass. Lancaster, Pa.

Biol. Rev. Biological Reviews and Proceedings of the Cambridge Philosophical Society.

Boll. Ist. sieroter., Milano. Bollettino dell'Istituto sieroterapico milanese. Milano.

Boll. Soc. ital. Biol. sper. Bollettino della Società italiana di biologia sperimentale. Milano.

Boston med. surg. J. Boston Medical and Surgical Journal. Boston.

*Brasil-med.** Brasil-medico. Rio de Janeiro.

Brit. J. exp. Path. British Journal of Experimental Pathology. London.

Brit. J. Ophthal. British Journal of Ophthalmology. London.

Brit. J. Surg. British Journal of Surgery. Bristol.

Brit. med. J. British Medical Journal. London.

*Brit. orthopt. J.** British Orthoptic Journal. Shrewsbury.

Brooklyn med. J. Brooklyn Medical Journal. Brooklyn.

Brux. méd. Bruxelles médical. Bruxelles.

Buffalo med. J. Buffalo Medical and Surgical Journal. Buffalo.

Bull. Acad. Méd. Belg. Bulletin de l'Académie royale de médecine de Belgique. Bruxelles.

Bull. Acad. Méd. Paris. Bulletin de l'Académie de médecine. Paris.

Bull. Amer. Hosp. Ass. Bulletin of the American Hospital Association, Chicago, Illinois.

Bull. Ass. belge Méd. soc. Bulletin de l'Association belge de Médecine sociale. Bruxelles.

Bull. gén. Thér., Paris. Bulletin général de thérapeutique médicale, chirurgicale, obstétricale et pharmaceutique. Paris.

*Bull. Hist. Med.** Bulletin of the History of Medicine. Baltimore.

*Bull. Hosp. Jt Dis., N. Y.** Bulletin of the Hospital of Joint Diseases, New York.

Bull. Hyg., Lond. Bulletin of Hygiene. London.

Bull. Laryng., Paris. Bulletin de laryngologie, otologie et rhinologie. Paris.

*Bull. Los Angeles neurol. Soc.** Bulletin of the Los Angeles Neurological Society. Los Angeles.

*Bull. math. Biophys.** Bulletin of Mathematical Biophysics. Colorado Springs, Colo.

Bull. méd., Paris. Bulletin médical. Paris.

Bull. méd. Québec. Bulletin médical de Québec. Quebec.

*Bull. Menninger Clin.** Bulletin of the Menninger Clinic. Topeka.

Bull. N. Y. Acad. Med. Bulletin of the New York Academy of Medicine. New York.

*Bull. N. Y. publ. Libr.** Bulletin of the New York Public Library. Astor, Lenox and Tilden Foundations. New York.

Bull. nav. med. Ass. Japan. Bulletin of the Naval Medical Association of Japan. Tokyo.

*Bull. Soc. Acclim.** Bulletin mensuel de la Société d'Acclimatation. Paris.

Bull. Soc. Anthrop. Paris. Bulletin et mémoires de la Société d'anthropologie de Paris.

Bull. Soc. franç. Ophtal. Bulletin et mémoires de la Société française d'ophtalmologie. Paris.

Bull. Soc. méd. Hôp. Paris. Bulletins et mémoires de la Société medicale des hôpitaux de Paris. Paris.

Bull. Soc. méd. Yonne. Bulletin de la Société medicale de l'Yonne. Auxerre.

Bull. Soc. nat. Chir. Bulletins et mémoires de la Société nationale de chirurgie. Paris.

Bull. Soc. Ophtal. Paris. Bulletin de la Société d'ophtalmologie de Paris. Paris.

Bull. Soc. Pédiat. Paris. Bulletin de la Société de pédiatrie de Paris. Paris.

*Bull. War. Med.** Bulletin of War Medicine. London.

*BuMed. News Lett., Wash.** U. S. Navy Department. BuMed. News Letter. Washington, D. C. [Restricted military publication.]

*BuMed. News Lett., Wash., Aviat. Suppl.** U. S. Navy Department. BuMed. News Letter, Aviation Supplement. Washington, D. C. [Restricted military publication.]

*Bur. nav. Pers. Inform. Bull.** Bureau of Naval Personnel Information Bulletin. Washington, D. C.

*Byull. eksp. Biol. Med.** Byulletin eksperimentalnoy biologii i meditsiny. Moskva.

C. R. Acad. Sci., Paris. Compte rendu hebdomadaire des séances de l'Académie des sciences. Paris.

C. R. Ass. franç. Av. Sci. Compte rendu de l'Association française pour l'avancement des sciences. Paris.

C. R. Soc. Biol. Paris. Compte rendu hebdomadaire des séances et mémoires de la Société de biologie. Paris.

Cairo sci. J. The Cairo Scientific Journal. Giza.

Calif. West. Med. California and Western Medicine. San Francisco.

Canad. med. Ass. J. Canadian Medical Association Journal. Montreal.

Čas. Lék. čes. Časopis Lékařův Českých. v Praze.
Cervello. Cervello. Giornale di neurologia. Napoli.
Chem. Abstr. Chemical Abstracts. Easton, Pa.
*Chicago med. J.** Chicago medical journal. A monthly record of medicine, surgery and collateral sciences. Chicago.
Chicago med. Rec. Chicago Medical Recorder. Chicago.
Chim. et Industr. Chimie et industrie. Paris.
*Chin. Imp. marit. Cust. med. Rep.** China. Imperial Maritime Customs. Medical Reports. Shanghai.
Cincinn. Lancet-Clin. Cincinnati Lancet-Clinic. Cincinnati.
Cleveland med. Gaz. Cleveland Medical Gazette. Cleveland.
Cleveland med. J. Cleveland Medical Journal. Cleveland.
Clin. J. Clinical Journal. London.
*Clín. mod.** La clínica moderna. Revista quincenal de medicina y cirugía. Zaragoza.
Clin. Rev. Clinical Review, Chicago.
Clin. Sci. Clinical Science, incorporating Heart. London.
Clinique, Brux. Clinique, Bruxelles.
Clinique, Paris. Clinique. Paris.
*Collier's** Collier's, the national weekly. Toronto.
*Congr. franç. Med.** Congrès Français de Médecine Paris.
*Conn. med. J.** Connecticut State Medical Journal. Hartford.
Contr. Embryol. Carneg. Instn. Contributions to Embryology. (Publications of the Carnegie Institution.) Washington.
Cron. Clin. med. Cronaca della clinica medica. Genova.
Curr. Res. Anesth. Current Researches in Anesthesia and Analgesia. Elmira, N. Y.
Czas. lek., Łódź. Czasopismo lekarskie. Łódź.

Diet. Hyg. Gaz. Dietetic and Hygienic Gazette. New York.
Difesa soc. Difesa sociale. Organo dell'Istituto Nazionale Fascista della Previdenza Sociale. Roma.
Dinglers J. Dinglers polytechnisches Journal. Berlin.
*Dis. Chest.** Diseases of the Chest. El Paso.
Discovery Rep. Discovery Reports. Gt. Britain, Colonial Office, Discovery Committee. London.
Dtsch. Arch. klin. Med. Deutsches Archiv für klinische Medizin. Berlin.
Dtsch. Klin. Deutsche Klinikam Eingange des zwanzigsten Jahrhunderts. Berlin.
Dtsch. med. Wschr. Deutsche medizinische Wochenschrift. Leipzig.
*Dtsch. Militärarzt.** Deutsche Militärarzt. Monatsschrift für die Sanitätsoffiziere des Heeres, des Kriegsmarine und der Luftwaffe. Berlin.
*Dtsch. Rev.** Deutsche Revue. Stuttgart.
Dtsch. Vjschr. öff. GesundhPfl. Deutsche Vierteljahrsschrift für öffentliche Gesundheitspflege. Braunschweig.
Dtsch. Z. Chir. Deutsche Zeitschrift für Chirurgie. Berlin.
Dtsch. Z. ges. gerichtl. Med. Deutsche Zeitschrift für die gesamte gerichtliche Medizin. Berlin.
*Dublin Hosp. Gaz.** Dublin Hospital gazette; a journal for the cultivation and improvement of practical medicine and surgery. Dublin.
Dublin J. med. Sci. Dublin Journal of Medical Science. Dublin.
Duodecim. Duodecim. Kirjoituksia lääketieteen ja lääkarintoiminnan aloilta. Helsinki.

*Edinb. med. surg. J.** Edinburgh Medical and Surgical Journal. Edinburgh.
*Eksper. Med., Kharkov.** Eksperimentalna meditsina. Médecine expérimentale. Kharkov.
Elect. Engng, N. Y. Electrical Engineering. New York.
Engng News. Engineering News. New York.
Ergebn. inn. Med. Kinderheilk. Ergebnisse der inneren Medizin u. Kinderheilkunde. Berlin.
Ergebn. Physiol. Ergebnisse der Physiologie. München.

*Fed. Proc. Amer. Soc. exp. Biol.** Federation Proceedings. Federation of American Societies for Experimental Biology. Baltimore.
Finska LäkSällsk. Handl. Finska Läkaresällskapets Handlingar. Helsingfors.
Fisiol. e. Med. Fisiol e medicina. Roma.
*Fiziol. Zh. S. S. S. R.** Fiziologicheskiy zhurnal. S. S. S. R. Moskva. Journal of Physiology of the U. S. S. R. Moscow.
*Flight Surg. Top.** Flight Surgeon Topics. Randolph Field, Texas.
Flying, N. Y. Flying. New York.
Folia haemat., Lpz. Folia haematologica. Leipzig.
Folia med., Napoli. Folia medica. Napoli.
Fortschr. Med. Fortschritte der Medizin. Berlin.
Fortschr. Röntgenstr. Fortschritte auf dem Gebiete der Röntgenstrahlen. Leipzig.

G. Clin. med. Giornale di clinica medica. Parma.
Gac. méd. catal. Gaceta médica catalana. Barcelona.
Gaz. hebd. Méd. Chir. Gazette hebdomadaire de médecine et de chirurgie. Paris.
Gaz. hebd. Sci. méd. Gazette hebdomadaire des sciences médicales de Bordeaux.
Gaz. Hôp., Paris. Gazette des hôpitaux civils et militaires. (La lancette française.) Paris.
Gaz. lek. Gazeta lekarska. Warszawa.
*Gaz. méd. Lyon.** Gazette médicale de Lyon. Lyon.
Gaz. méd. Paris. Gazette médicale de Paris.
Gas. méd. Strasbourg. Gazette médicale de Strasbourg. Strasbourg.
Gazz. int. med.-chir. Gazzetta internazionale medicochirurgica, igiene e di interissi professionali. Napoli.
Gazz. med. ital. Gazzeta medica italiana. Torino.
*Gazz. med. ital. Prov. Venete.** Gazzetta medica italiana. Provincie Venete. Padova.
Gazz. med. lombarda. Gazzetta medica lombarda. Milano.
Gazz. med. Roma. Gazzetta medica di Roma. Milano.
Gazz. Osp. Clin. Gazzetta degli ospedali e delle cliniche. Milano.

Geneesk. Tijdschr. Ned.-Ind. Geneeskundig tijdschrift voor Nederlandsch-Indië. Batavia.
Gesundheit, Lpz. Gesundheit. Zeitschrift für öffentliche und private Hygiene. Leipzig.
Gesundheitsing. Gesundheitsingenieur. Berlin.
Gigiena Truda. Gigiena truda. Moskva.
Glasg. med. J. Glasgow Medical Journal. Glasgow.
*Göschens Dtsch. Klin.** Deutsche Klinik. Zeitung für Beobachtungen aus deutschen Kliniken und Krankenhäusern. Herausgegeben von Alexander Göschen. Berlin.
Gyógyászat. Gyógyászat. Budapest.

Hahnemann. Mon. Hahnemannian Monthly. Philadelphia.
*Handb. Hyg.** Handbuch der Hygiene. Jena.
*Handb. Neurol. Ohres.** Handbuch der Neurologie des Ohres. Herausgegeben von G. Alexander und O. Marburg. Berlin, Urban und Schwarzenberg.
*Handb. spec. Path. Ther.** Handbuch der speciellen Pathologie und Therapie. Herausgegeben von H. von Ziemssen, Leipzig. F. C. W. Vogel.
*Hannoversche Ann. ges. Heilk.** Hannoversche Annalen für die gesammte Heilkunde. Hannover.
*Hist. Acad. Sci., Paris.** Histoire de l'academie des sciences. Paris.
Hôpital. Hôpital. Paris.
Hoppe-Seyl. Z. Hoppe-Seyler's Zeitschrift für physiologische Chemie. Berlin.
*Hosp. Cps Quart.** Hospital Corps Quarterly. The Supplement to the United States Naval Medical Bulletin. Washington, D. C.
Hospital. Hospital. Journal of the medical sciences and hospital administration. London.
Hospitalstidende. Hospitalstidende. Kjøbenhavn.
Hot Springs med. J. Hot Springs Medical Journal. Hot Springs, Arkansas.
Hyg. gén. appl. L'hygiène générale et appliquée. Paris.
Hyg. Rdsch. Hygienische Rundschau. Berlin.
Hyg. Zbl. Hygienisches Zentralblatt. Leipzig.
Hygeia, Chicago. Hygeia. Chicago.
Hygiea, Stockh. Hygiea. Stockholm.

Ill. Mschr. ärztl. Polyt. Illustrirte Monatsschrift der ärztlichen Polytechnik. (Zeitschrift f. Krankenpflege Suppl.) Berlin.
Illinois med. J. Illinois Medical Journal. Chicago.
*Ind. med. J.** Indiana Medical Journal. Indianapolis.
Indép. méd., Paris. L'indépendence médicale. Paris.
Indian med. Gaz. Indian Medical Gazette. Calcutta.
Indian med. Rec. Indian Medical Record. Calcutta.
Industr. Engng Chem. Industrial and Engineering Chemistry. Easton, Pa.
Industr. Hyg. Bull. Industrial Hygiene Bulletin. Department of Labor. New York State. New York.
Industr. Med. Industrial Medicine. Chicago.
Inform. Circ. U. S. Bur. Min. Information Circular. U. S. Bureau of Mines. Washington.
Int. Air Congr. International Air Congress.
Int. Clin. International Clinics. Philadelphia.
Int. Congr. Hyg. (Demogr.) International Congress on Hygiene (and Demography.).
Int. Congr. Med. International Congress of Medicine.
Irish J. med. Sci. Irish Journal of Medical Science. Dublin.

J. acoust. Soc. Amer. Journal of the Acoustical Society of America. Menasha, Wis.
J. Amer. chem. Soc. Journal of the American Chemical Society. Washington, D. C.
J. Amer. Inst. Homoeop. Journal of the American Institute of Homoeopathy. Chicago.
J. Amer. med. Ass. Journal of the American Medical Association. Chicago.
J. Amer. pharm. Ass. Journal of the American Pharmaceutical Association. Baltimore.
J. Anat., Paris. Journal de l'anatomie et de la physiologie normales et pathologiques de l'homme et des animaux. Paris.
J. appl. Psychol. Journal of Applied Psychology. Worcester, Mass.
J. Ass. milit. Surg. U. S. Journal of the Association of Military Surgeons of the United States, Carlisle, Pa.
J. Aviat. Med. Journal of Aviation Medicine. St. Paul.
J. Bact. Journal of Bacteriology. Baltimore.
J. biol. Chem. Journal of Biological Chemistry. Baltimore.
J. Bone Jt Surg. Journal of Bone and Joint Surgery. Boston.
J. Boston Soc. med. Sci. Journal of the Boston Society of Medical Sciences. Boston.
*J. Canad. med. Serv.** Journal of the Canadian Medical Services. Ottawa.
J. cell. comp. Physiol. Journal of Cellular and Comparative Physiology. Philadelphia.
J. chem. Soc. Journal of the Chemical Society. London.
J. Chosen med. Ass. Journal of the Chosen Medical Association. Keijo.
J. clin. Invest. Journal of Clinical Investigation. Lancaster, Pa.
*J. Conn. méd. prat.** Journal des connaissances médicales pratiques et de pharmacologie. Paris.
J. Egypt. med. Ass. Journal of the Egyptian Medical Association. Cairo.
J. Elisha Mitchell sci. Soc. Journal of the Elisha Mitchell Scientific Society. Chapel Hill, N. C.
J. exp. Med. Journal of Experimental Medicine. New York.
J. exp. Psychol. Journal of Experimental Psychology. Evanston, Ill.
J. Franklin Inst. Journal of the Franklin Institute. Philadelphia.
J. gen. Physiol. Journal of General Physiology. Baltimore.
J. Hyg., Camb. Journal of Hygiene. Cambridge.
J. Indiana med. Ass. Journal of the Indiana State Medical Association. Indianapolis.
J. industr. Engng Chem. Journal of Industrial and Engineering Chemistry. Easton, Pa.

J. industr. Hyg. Journal of Industrial Hygiene and Toxicology. Baltimore.
J. infect. Dis. The Journal of Infectious Diseases. Chicago.
J. Kans. med. Soc. Journal of the Kansas Medical Society. Columbus.
J. Kumamoto med. Soc. Journal of the Kumamoto Medical Society, Japan.
J. Lab. clin. Med. Journal of Laboratory and Clinical Medicine. St. Louis.
J. Lancet. Journal Lancet. Minneapolis.
J. Laryng. Journal of Laryngology (Rhinology) and Otology. London.
J. Mammal. Journal of Mammalogy. Baltimore.
J. Méd. Bordeaux. Journal de médecine de Bordeaux.
J. méd. Brux. Journal médicale de Bruxelles. Bruxelles.
*J. méd. Chir. Pharm.** Journal de médecine de chirurgie et de pharmacologie. Bruxelles.
J. Méd. Chir. prat. Journal de médecine et de chirurgie pratiques. Paris.
J. Méd. Lyon. Journal de médecine de Lyon.
J. Méd. Paris. Journal de médecine de Paris.
J. med. Res. Journal of Medical Research. Boston.
J. med. Soc. N. J. The journal of the medical society of New Jersey. Orange, New Jersey.
J. metab. Res. Journal of Metabolic Research. Morristown, N. J.
J. Mich. med. Soc. Journal of the Michigan State Medical Society. Muskegon.
*J. Mt Sinai Hosp., N. Y.** Journal of Mount Sinai Hospital. New York.
J. nerv. ment. Dis. Journal of Nervous and Mental Diseases. New York.
J. Neurol. Psychopath. Journal of Neurology and Psychopathology. London.
*J. Neurophysiol.** Journal of Neurophysiology. Springfield, Ill.
J. Okayama med. Soc. Journal of the Okayama Medical Society. Okayama Igakkai Zasshi. Okayama.
J. opt. Soc. Amer. Journal of the Optical Society of America. New York.
J. Path. Bact. Journal of Pathology and Bacteriology London; Edinburgh.
J. Pharm. Chim., Paris. Journal de pharmacie et de chimie. Paris.
J. Pharmacol. Journal of Pharmacology and Experimental Therapeutics. Baltimore.
J. Physiol. Journal of Physiology. London; Cambridge.
J. Physiol. Path. gén. Journal de physiologie et de pathologie générale. Paris.
J. Psychol. Journal of Psychology. Provincetown, Mass.
J. R. Army med. Cps. Journal of the Royal Army Medical Corps. London.
J. R. nav. med. Serv. Journal of the Royal Naval Medical Service. London.
J. R. sanit. Inst. Journal of the Royal Sanitary Institute. London.
*J. R. Soc. Arts.** Journal of the Royal Society of Arts. London.
J. Radiol. Électrol. Journal de Radiologie et D'Électrologie. Revue médicale mensuelle. Paris.
*J. Sci. méd. Louvain.** Journal des sciences médicales de Louvain.
J. Soc. chem. Ind., London. Journal of the Society of Chemical Industry. London.
J. State Med. Journal of State Medicine. London.
*J. Thér.** Journal de Thérapeutique. Paris.
J. thorac. Surg. Journal of Thoracic Surgery. St. Louis.
J. trop. Med. (Hyg.). Journal of Tropical Medicine (and Hygiene). London.
Janus. Janus. Archives internationales pour l'histoire de la medécine. Amsterdam, Paris.
Jap. J. med. Sci. Japanese Journal of Medical Sciences. Transactions and Abstracts. Tokyo.
Jb. Kinderheilk. Jahrbuch für Kinderheilkunde und physische Erziehung. Berlin.
Jb Psychiat. Neurol. Jahrbücher für Psychiatrie und Neurologie. Leipzig und Wien.
Jber. Ges. Naturk. Dresden. Jahresbericht der Gesellschaft für Natur- u. Heilkunde in Dresden.
Johns Hopk. Hosp. Bull. Johns Hopkins Hospital Bulletin. Baltimore.

Klin. Mbl. Augenheilk. Klinische Monatsblätter für Augenheilkunde. Stuttgart.
Klin. Med., Mosk. Klinicheskaya meditsina. Moskva.
Klin.-ther. Wschr. Klinisch-therapeutische Wochenschrift. Berlin.
Klin. Wschr. Klinische Wochenschrift. Berlin.
Kolloidchem. Beih. Kolloidchemische Beihefte. (Ergänzungshefte zur Kolloid-Zeitschrift.) Dresden.
*KorrespBl. Ärz. Apothek. Oldenb.** Correspondenz-Blatt für die Aerzte und Apotheker des Grossherzogthums Oldenburg. Oldenburg.
Krankenpflege, Berl. Krankenpflege. Berlin.

Lancet. Lancet, London.
Laryngoscope, St Louis. Laryngoscope. St. Louis.
Lehigh med. Mag. Lehigh Valley Medical Magazine. Easton, Pa.
Lek. wojsk. Lekarz Wojskowy. Warszawa.
*L'expérience.** L'expérience. Journal de médecine et de chirurgie. Paris.
*Literary Dig.** Literary Digest. New York.
*Lond. med. phys. J.** London Medical and Physical Journal. London.
*Lond. med. Recorder.** London Medical Recorder. London.
Long Is. med. J. Long Island Medical Journal. Brooklyn, N. Y.
Luftfahrtforsch. Luftfahrtforschung. München.
*Luftfahrtmed.** Luftfahrtmedizin. Berlin.
*Luftfahrtmed. Abh.** Luftfahrtmedizinische Abhandlungen. Leipzig.
Lyon méd. Lyon médicale. Lyon.

*Maandschr. Kindergeneesk.** Maandschrift voor Kindergeneeskunde. Leiden.
Maine med. J. Maine Medical Journal. Portland.

Marit. med. News. Maritime Medical News. Halifax, N. S.
Marseille méd. Marseille médical. Marseille.
Maryland med. J. Maryland Medical Journal. Baltimore.
*Med. Arch., St. Louis.** The Medical Archives. St. Louis.
Med. Brief. Medical Brief. St. Louis.
Med. Bull., Philad. Medical Bulletin. Philadelphia.
Med. Century. Medical century. New York
*Med.-chir. Rev.** Medico-Chirurgical Review, and Journal of Practical Medicine. London.
Med. Chron. Medical Chronicle. Manchester.
Med. Clin. N. Amer. Medical Clinics of North America. Philadelphia.
Med. d. Lavoro. Medicina del lavoro. Milano.
*Med. Exam. Rec. med. Sci.** Medical Examiner and Record of Medical Science. Philadelphia.
Med. Her. The Medical Herald and Physiotherapist, incorporating the Medical Fortnightly & Laboratory News. St. Louis Clinique, General Practitioner and The Kansas City Medical Index-Lancet. Kansas City, Missouri.
Med. Infort. Lav. Medicina degli infortuni del lavoro e delle malattie professionali. Perugia.
Med. J. Aust. Medical Journal of Australia. Sydney.
*Med. Jb., Wien.** Medizinische Jahrbücher. Wien.
Med. Klinik. Medizinische Klinik. Berlin.
Med. KorrBl. Württemb. Medicinisches Korrespondenzblatt des Wuerttembergischen aerztlichen Landesvereins. Stuttgart.
Med. News, N. Y. Medical News. New York.
*Med. News, Philad.** Medical News. Philadelphia.
Med. Pr. Medical Press and Circular. London.
*Med. Pr. west. N. Y.** Medical Press of western New York. Buffalo.
Med. Rec., N. Y. Medical Record. New York. (East Rutherford, N. J.).
*Med. Reporter.** Medical reporter. A record of medicine, surgery, public health, and of general medical intelligence. Calcutta.
*Med. Res. Coun. (Grt. Brit.), Spec. Rep. Ser.** Medical Research Council. Great Britain. Special Report Series. London.
Med. Rev., Bergen. Medicinsk Revue. Bergen.
Med. Stand. Medical Standard, Chicago.
Med. Times. Lond. Medical Times and Hospital Gazette. London.
Med. Trib. Medical Tribune. New York.
Med. Weekbl. Medisch Weekblad voor Noord- en Zuid- Nederland. Amsterdam.
Med. Welt. Medizinische Welt. Berlin.
Médicine. Médicine. Paris.
Medicine. Baltimore. Medicine. Baltimore.
Medits. Pribavl. Meditsinskia pribavlenia k morskomu sborniku. St. Petersburg.
Mem. Boston Soc. nat Hist. Memoirs of the Boston Society of Natural History. Boston.
*Mém. Soc. Méd. Nancy.** Mémoires de la Société de Médicine de Nancy. Nancy.
*Mém. Soc. Méd. Strasbourg.** Mémoires de la Société de Médicine de Strasbourg. Strasbourg.
*Mem. Soc. Sci. nat., Cherbourg.** Memoires de la société des sciences naturelles de Cherbourg.
Memorabilien. Memorabilien. Zeitschrift für rationelle praktische Arzte. Heilbronn.
Memphis med. J. Memphis Medical Journal. Memphis.
Middlesex Hosp. Rep. Reg. Middlesex Hospital. Reports of the Medical, Surgical and Pathological Registrars. London.
Milit. Surg. Military Surgeon. Washington.
Min. Proc. Instn. civ. Engrs. Minutes of Proceedings of the Institution of Civil Engineers. London.
*Minerva med., Torino.** Minerva medica. Torino.
Minn. Med. Minnesota Medicine. St. Paul.
Miss. Vall. med. J. Mississippi Valley Medical Journal. Louisville, Ky.
Mitt. med. Akad. Kioto. Mitteilungen aus der Medizinischen Akademie zu Kioto. Kyoto-Ikadaigaku-Zasshi.
Mitt. med. Ges. Tokio. Mitteilungen der Medizinischen Gesellschaft zu Tokio.
Mod. Hosp. Modern Hospital. Chicago.
Molkereiztg. Berl. Molkerizeitung. Berlin.
Montpellier méd. Montpellier médical. Montpellier.
Morgagni. Morgagni. Giornale di scienze mediche. Milano.
Mschr. Ohrenheilk. Monatsschrift für Ohrenheilkunde und Laryngo-Rhinologie. Wien.
Mschr. Unfallheilk. Monatsschrift für Unfallheilkunde und Invalidenwesen. Leipzig.
*Mschr. Unfallheilk. Versicherungsmed.** Monatsschrift für Unfallheilkunde und Versicherungsmedizin. Berlin.
Münch. med. Wschr. Münchener medizinische Wochenschrift. München.

*N. C. med. J.** North Carolina Medical Journal. Winston-Salem, N. C.
*N. Orleans med. surg. J.** New Orleans Medical and Surgical Journal. New Orleans.
N. S. med. Bull. Nova Scotia Medical Bulletin. Halifax.
*N. Y. J. Med.** New York Journal of Medicine and the Collateral Sciences. New York.
N. Y. med. J. New York Medical Journal. New York.
N. Y. St. J. Med. New York State Journal of Medicine. New York.
*Nat. Serv.** National Service. New York.
Nature, Lond. Nature. London.
Nature, Paris. Nature. Paris.
Naturwissenschaften. Naturwissenschaften. Berlin.
Nav. med. Bull., Wash. Naval Medical Bulletin. Washington.
Ned. milit.-geneesk. Arch. Nederlandsch militair-geneeskundig archief. Utrecht.
Ned. Tijdschr. Geneesk. Nederlandsch tijdschrift voor geneeskunde. Amsterdam.
*Nelson Loose-leaf Medicine.** Nelson new loose-leaf medicine. New York, etc., Thomas Nelson and Sons.

*Nelson Loose-leaf Surgery.** Nelson new loose-leaf surgery. New York, etc., Thomas Nelson and Sons.
Nevrol. Vyestn. Nevrologicheskii vestnik. Kazan.
New Engl. J. Med. New England Journal of Medicine. Boston.
*New-Engl. J. Med. Surg.** New-England Journal of Medicine and Surgery, and Collateral Branches of Science. Boston.
*Nord. Med., Stockholm.** Nordisk medicin. Stockholm.
*Normandie méd.** Normandie médicale. Rouen.
Norsk Mag. Laegevidensk. Norsk Magazin for Laegevidenskaben. Oslo.
Northumb. Durh. med. J. Northumberland and Durham Medical Journal. Newcastle.
Not. Proc. roy. Instn. Notices of the Proceedings at the Meetings of the Members of the Royal Institution. London.
Nothnagel's spec. Path. Ther. Specielle Pathologie und Therapie. Herausgegeben von Hermann Nothnagel. Wien, Alfred Hölder. 2. Aufl.
Nouv. Reméd. Nouveaux remèdes. Paris.
Nuova Riv. Clin. Assist. psich. Nuova rivista di clinica ed assistenza psichiatrica e di terapia applicata. Roma.

Öst. ärztl. VerZtg. Österreichische ärztliche Vereinszeitung. Wien.
Öst. ChemZtg. Österreichische Chemikerzeitung u. Zeitschr. f. Nahrungsmitteluntersuchung, Hygiene u. Warenkunde. Wien.
*Öst. Jb. Paediat.** Österreichisches Jahrbuch für Paediatrik. Wien.
Öst. Sanitätsw. Österreichische Sanitätswesen. Wien.
*Öst.-ung. BadeZtg.** Österreichisch-ungarische Bade-Zeitung. Wien.
Öst. Vjschr. Cesundh.-Pfl. Österreichische Vierteljahrsschrift für Gesundheitspflege. Wien und Berlin.
*Öst. Z. prakt. Heilk.** Österreichische Zeitschrift für Praktische Heilkunde. Wien.
Ohio St. med. J. Ohio State Medical Journal Columbus.
Okayama Igakkai Zasshi, see *J. Okayama med. Soc.*
Old Dom. J. Med. Surg. Old Dominion Journal of Medicine and Surgery, Richmond. Virginia.
*Ophthalmologica.** Ophthalmologica. Basel.
Orv. Hetil. Orvosi Hetilap. Honi és külföldi gyógyázat és kórbuvárlat közlönye. Budapest.
*Oss. med., Palermo.** Osservatore medico. Giornale Siciliano. Palermo.
*Oto-rino-laring. ital.** Oto-rino-laringologia italiana. Bologna.

*Pacific Sci. Congr.** Pacific Science Congress.
Paris méd. Paris médical. La semaine du clinicien. Paris.
Penn. Hosp. Rep. Pennsylvania Hospital Reports. Philadelphia.
Penn. med. J. Pennsylvania Medical Journal. Pittsburgh.
*Peoria med. Mon.** Peoria medical monthly. Peoria.
Pester med.-chir. Pr. Pester medizinisch-chirurgische Presse. Budapest.
Pflüg. Arch. ges. Physiol. Pflügers Archiv für die gesamte Physiologie des Menschen und der Tiere. Berlin.
Philad. med. J. Philadelphia Medical Journal. Philadelphia.
Philos. Trans. Philosophical Transactions of the Royal Society. London.
Phys. & Surg., Ann Arbor. Physician and Surgeon. Ann Arbor, Mich.
Phys. Z. Physikalische Zeitschrift. Leipzig.
Physiol. Abstr. Physiological Abstracts, London.
Physiol. Rev. Physiological Reviews. Baltimore.
*Physiol. Zoöl.** Physiological Zoölogy. Chicago.
Policlinico. Policlinico. Roma.
Polsk. Gaz. lek. Polska Gazeta lekarska. Lwów.
*Polsk. Przegl. Med. Lotn.** Polski przegląd medycyny lotniczej. Warszawa. Revue polonaise de la médecine aéronautique. Varsovie.
*Polyclinic.** Polyclinic. Philadelphia.
Pr. méd. Presse médicale. Paris.
Practitioner. Practitioner. London.
Prag. med. Wschr. Prager medicinische Wochenschrift. Prag.
Prakt. Arzt. Praktische Arzt. Leipzig; Wetzlar.
*Prat. méd.** Pratique médicale. Paris.
*Prat. méd., Paris.** Pratique médicale. Journal des oreilles, du nez et du larynx. Paris.
*Proc. Amer. Soc. civil Engrs.** Proceedings of the American Society of Civil Engineers. New York.
*Proc. cent. Soc. clin. Res.** Proceedings of the Central Society for Clinical Research. Chicago.
Proc. Mayo Clin. Proceedings of the Staff Meetings of the Mayo Clinic. Rochester, Minn.
Proc. N. Y. path. Soc. Proceedings of the New York Pathological Society. New York.
Proc. nat. Acad. Sci., Wash. Proceedings of the National Academy of Sciences. Washington.
Proc. Philad. Co. med. Soc. Proceedings of the Philadelphia County Medical Society. Philadelphia.
Proc. R. Soc. Med. Proceedings of the Royal Society of Medicine. London.
Proc. roy. Soc. Proceedings of the Royal Society. London.
Proc. roy. Soc. Edinb. Proceedings of the Royal Society of Edinburgh.
Proc. Soc. exp. Biol., N. Y. Proceedings of the Society for Experimental Biology and Medicine. New York (Utica, N. Y.)
Proc. U. S. nav. Inst. Proceedings of the United States Naval Institute. Annapolis, Md.
Progr. méd., Paris. Progrès medical. Paris.
Psychiat.-neurol. Wschr. Psychiatrisch-Neurologische Wochenschrift. Halle a. S.
Psychiat. Quart. Psychiatric Quarterly. Utica, N. Y.
Psychol. Abstr. Psychological Abstracts. Lancaster, Pa.
Psychol. Bull. Psychological Bulletin. Evanston, Ill.
Psychol. Forsch. Psychologische Forschung. Berlin.

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Psychol. Rev. Psychological Review. Evanston, Ill.

*Psychosom. Med.** Psychosomatic Medicine. Experimental and Clinical Studies. Washington.

Publ. Cornell Univ. med. Coll. Publications of Cornell University Medical College. New York.

Publ. Hlth Bull., Wash. Public Health Bulletin. Washington.

Publ. Hlth J., Toronto. Public Health Journal. Toronto.

*Publ. Hlth Nurs.** Public Health Nursing. New York.

Publ. Hlth Rep., Wash. Public Health Reports. Washington.

Quart. Bull. Nthwest. Univ. Quarterly Bulletin of Northwestern University. (b) Medical. Evanston, Ill.

Quart. J. exp. Physiol. Quarterly Journal of Experimental Physiology. London.

Quart. J. Med. Quarterly Journal of Medicine. Oxford.

Quart. J. R. met. Soc. Quarterly Journal of the Royal Meteorological Society. London.

R. C. Accad. Lincei. Atti della reale Accademia dei Lincei. Rendiconti. Classe di scienze fisiche, matematiche e naturali. Roma.

R. C. Ist. lombardo. Rendiconti dell'Istituto lombardo di scienze e lettere. Milano.

Radiology. Radiology. Syracuse, N.Y.

Ramazzini. Il Ramazzini. Giornale Italiano di medicina sociale. Firenze.

*Rass. Fisiopatol. clin. terap.** Rassegna di fisiopatologia clinica e terapeutica. Pisa.

Rass. Med. Lav. industr. Rassegna di medicina applicata al lavoro industriale. Torino.

*Rass. Sci. med.** Rassegna di scienze mediche. Modena.

Rep. Brit. Ass. Report of the British Association for the Advancement of Science. London.

*Rep. Invest. U.S. Bur. Min.** Reports of Investigations. U.S. Bureau of Mines. Washington.

Rép. Thér. Répertoire de thérapeutique. Formules et médications nouvelles. Paris.

Rev. Asoc. méd. argent. Revista de la Asociación médica argentina. Buenos Aires.

*Rev. brasil. Biol.** Revista brasileira de Biologia. Rio de Janeiro, D. F.

Rev. Chir., Paris. Revue de chirurgie. Paris.

Rev. Cienc. méd., Barcelona. Revista de Ciencias Médicas de Barcelona. Barcelona.

*Rev. deux Mondes.** Revue des deux mondes. Paris.

Rev. filipina Med. Revista filipina de medicina y farmacia. Manila.

*Rev. Gastroenterol.** Review of Gastroenterology. New York.

Rev. gén. Clin. Revue générale de clinique et de thérapeutique. Paris.

Rev. gén. Sci. pur. appl. Revue générale des sciences pures et appliquées. Paris.

Rev. Hyg. Police sanit. Revue d'hygiène et de police sanitaire (et de médecine préventive). Paris.

Rev. Hyg. thér. Revue d'hygiène thérapeutique. Paris.

Rev. Laryng., Paris. Revue de laryngologie, d'otologie et de rhinologie. Paris. (Bordeaux.)

Rev. Med. Cirug. Habana. Revista de medicina y cirugía de la Habana. Habana.

Rev. méd., Cordoba. Revista médica. Córdoba.

Rev. méd. Est. Revue médicale de l'Est. Nancy.

*Rev. méd. franç étrang.** Revue médicale française et étrangère; journal des progrès de la médecine Hippocratique. Paris.

Rev. Med. Hyg. milit., Rio de J. Revista de medicina e hygiene militar. Rio de Janeiro.

Rev. méd. Normandie. Revue médicale de Normandie. Rouen.

Rev. Médecine. Revue de Médecine. Paris.

*Rev. mex. Cirug. Ginec. Cánc.** Revista Mexicana de Cirugía, Ginecología y Cáncer. México, D. F.

Rev. Oftal. S. Paulo. Revista de oftalmologia de São Paulo.

Rev. Path. comp. Revue de pathologie comparée et d'hygiène générale. Paris.

Rev. Psychothér. Revue de psychothérapie et de psychologie appliquée. Paris.

*Rev. sanit. Bordeaux.** Revue sanitaire de Bordeaux et de la Provence. Bordeaux.

Rev. sci. Instrum. The Review of Scientific Instruments. Menasha.

Rev. sci., Paris. Revue scientifique. (Revue rose.) Paris.

Rev. Thér. méd.-chir. Revue de thérapeutique médico-chirurgicale. Paris.

Rif. med. Riforma medica. Napoli.

Riv. clin. Rivista clinica. Milano.

Riv. gen. Clin. med. Rivista generale italiana de clinica medica. Pisa.

Riv. ital. Neuropat. Rivista italiana di neuropatologia, psichiatria ed elettroterapia. Catania.

Riv. Med. leg. Rivista di medicina legale e di giurisprudenza medica. Siena.

Riv. osped. Rivista ospedaliera. Roma.

Riv. Pat. Clin. Tuberc. Rivista di patologia e clinica della tuberculosi. Bologna.

*Rocky Mtn med. J.** Rocky Mountain Medical Journal. Denver.

Röntgenpraxis. Röntgen-Praxis. Leipzig.

Russk. Vrach. Russkii vrach. St. Petersburg.

S. B. Akad. Wiss. Wien. Sitzungsberichte der Kais. Akademie der Wissenschaften in Wien.

S. B. Ges. Morph. Physiol. München. Sitzungsberichte der Gesellschaft für Morphologie und Physiologie in München.

S. B. Isis Dresden. Sitzungsberichte und Abhandlungen der Naturwissenschaftlichen Gesellschaft Isis in Dresden.

S. B. phys.-med. Soz. Erlangen. Sitzungsberichte der Physikalisch-medizinischen Sozietät in Erlangen.

S. B. preuss. Akad. Wiss. Sitzungsberichte der Kgl. Preussischen Akademie der Wissenschaften zu Berlin.

*Sacramento med. Times.** Sacramento Medical Times. Sacramento.

Samml. klin. Vortr. Sammlung klinischer Vorträge. (R. von Volkmann.) Leipzig.

Schweiz. ärztl. Mitt. Schweizerische ärztliche Mitteilungen, aus Universitätsinstituten. Zürich.

Schweiz. med. Wschr. Schweizerische medizinische Wochenschrift. Basel.

Sci. Amer. Suppl. Scientific American Supplement. New York.

Sci. Mon., N.Y. Scientific Monthly, New York.

Sci. News Lett., Wash. Science News Letter. Washington.

Sci. Progr. twent. Cent. Science Progress in the Twentieth Century. London.

Science. Science. New York.

Sei-i-Kwai med. J. Sei-i-Kwai Medical Journal Tokyo.

Sem Hôp. Paris. Semaine des hôpitaux de Paris.

Sem. méd., B. Aires. Semana médica. Buenos Aires.

*Sem. méd. españ.** Semana médica española. Madrid.

Sem. méd., Paris. Semaine médicale. Paris.

Sib. vrach. Gaz. Sibirskaya vrachebnaya gazeta. Irkutsk.

Sicilia med. Sicilia Medica. Palermo.

Siglo méd. Siglo médico. Madrid.

Skand. Arch. Physiol. Skandinavisches Archiv für Physiologie. Berlin.

*Sovetsk. Vrach. Zh.** Sovetskiy vrachebniy zhurnal. Leningrad.

Sperimentale. Sperimentale. Archivio di biologia normale e patologica. Firenze.

Spitalul. Spitalul. Bucuresti.

St Bart's Hosp. J. St. Bartholomew's Hospital Journal. London.

St Louis med. surg. J. St. Louis Medical and Surgical Journal. St. Louis.

*St Petersb. med. Wschr. (Z.).** St. Petersburger medizinische Wochenschrift. (Zeitschrift.)

*Sth. med. J., Birmingham.** Southern Medical Journal. Journal of the Southern Medical Association. Birmingham, Ala.

Strahlentherapie. Strahlentherapie. Berlin; Wien.

Surg. Clin. N. Amer. Surgical Clinics of North America, Philadelphia.

Surg. Gynec. Obstet. Surgery, Gynecology and Obstetrics. Chicago.

Surg. St Louis. Surgery. A monthly journal devoted to the art and science of surgery. St. Louis.

Tech. Pap. Bur. Min., Wash., Technical Papers. Bureau of Mines. Washington.

Tex. St. J. Med. Texas State Journal of Medicine. Fort Worth, Tex.

Ther. d. Gegenw. Therapie der Gegenwart. Berlin; Wien.

Ther. Gaz. Therapeutic Gazette. Detroit.

Ther. Mh. (Halbmh.) Therapeutische Monatshefte (Halbmonatshefte). Berlin.

*Tice's Practice of Medicine.** Practice of Medicine. Edited by Frederick Tice. Hagerstown, Md., W. F. Prior Company.

Tidskr. milit. Hälsov. Tidskrift i militär Hälsovård. Lund.

Tohoku J. exp. Med. Tohoku Journal of Experimental Medicine. Tokyo.

Tommasi. Il Tommasi. Giornale di biologia, medicina e chirurgia. Napoli.

Trans. Amer. Acad. Ophthal. Oto-laryng. Transactions of the American Academy of Ophthalmology and Oto-laryngology. Omaha.

Trans. Amer. climat. (clin.) Ass. Transactions of the American Climatological (and Clinical) Association. Saranac Lake, N. Y.

Trans. Amer. Inst. Homoeop. Transactions of the American Institute of Homoeopathy. New York.

Trans. Amer. med. Ass. Transactions of the American Medical Association. Philadelphia.

Trans. Amer. ophthal. Soc. Transactions of the American Ophthalmological Society. New York.

Trans. Amer. otol. Soc. Transactions of the American Otological Society. St Louis.

Trans. Amer. Soc. Heat. Vent. Engrs. Transactions of the American Society of Heating and Ventilating Engineers. New York.

Trans. Ass. Amer. Phys. Transactions of the Association of American Physicians. Philadelphia.

Trans. Coll. Phys. Philad. Transactions of the College of Physicians of Philadelphia, Philadelphia.

Trans. Colo. med. Soc. Transactions of the Colorado State Medical Society. Denver.

Trans. Edinb. obstetr. Soc. Transactions of the Edinburgh Obstetrical Society. Edinburgh.

Trans. Faraday Soc. Transactions of the Faraday Society. London.

Trans. Hunter. Soc. Transactions of the Hunterian Society. London.

*Trans. Ill. St. med. Soc.** Transactions of the Illinois State Medical Society. Chicago.

Trans. Illum. Engng Soc., N. Y. Transactions of the Illuminating Engineering Society. New York.

Trans. Instn Min. Engrs. Lond. Transactions of the Institution of Mining Engineers. London.

Trans. Kans. Acad. Sci. Transactions of the Kansas Academy of Science. Lawrence. Kans.

Trans. med.-chir. Soc. Edinb. Transactions of the Medico-Chirurgical Society of Edinburgh.

Trans. med. Soc. London. Transactions of the Medical Society of London.

Trans. med. Soc. St. N. Y. Transactions of the Medical Society of the State of New York. New York.

*Trans. N. Y. med. Ass.** Transactions of the New York State medical association. New York.

Trans. ophthal. Soc. U. K. Transactions of the Ophthalmological Society of the United Kingdom, London.

*Trans. R. Acad. Med. Ireland.** Transactions of the Royal Academy of Medicine in Ireland, Dublin.

Trans. R. Soc. trop. Med. Hyg. Transactions of the Royal Society of Tropical Medicine and Hygiene. London.

Travail hum. Travail humain. Paris.

Trib. med., Rio de J. Tribuna medica. Rio de Janeiro.

Ugeskr. Laeg. Ugeskrift for Laeger. Kjøbenhavn.

*Un. méd. Gironde.** Union médicale de la Gironde. Bordeaux.

*Un. méd., Paris.** L'Union médicale. Journal des intérêts scientifiques et pratiques moraux et professionnels du corps médical. Paris.

Univ. Durh. Coll. Med. Gaz. University of Durham College of Medicine Gazette. Durham.

Upsala LäkFören. Förh. Upsala Läkareförenings Förhandlingar. Upsala.

v. Graefes Arch. Ophthal. Albrecht von Graefes Archiv für Ophthalmologie. Berlin.

Valsalva. Valsalva. Rivista mensile di oto-rino-laringojatria. Roma.

Verh. dtsch. Ges. inn. Med. Verhandlungen der Deutschen Gesellschaft für Innere Medizin. München.

Verh. dtsch. Ges Kreislaufforsch. Verhandlungen der Deutschen Gesellschaft für Kreislaufforschung. Dresden.

Verh. dtsch. Kongr. inn. Med. Verhandlungen des Deutschen Kongresses für Innere Medizin. Wiesbaden.

Verh. dtsch. otol. Ges. Verhandlungen der Deutschen Otologischen Gesellschaft. Jena.

Verh. dtsch. path. Ges. Verhandlungen der Deutschen Pathologischen Gesellschaft. Jena.

Verh. Ges. dtsch. Naturf. Ärzt. Verhandlungen der Gesellschaft Deutscher Naturforscher und Ärzte. Leipzig.

Verh. Kongr. inn. Med. Verhandlungen des Kongresses für Innere Medizin. Wiesbaden.

Virchows Arch. Virchows Archiv für pathologische Anatomie und Physiologie und für klinische Medizin. Berlin.

Virginia med. (Semi-) Mon. Virginia medical (Semi-) Monthly. Richmond.

Vjschr. gerichtl. Med. Vierteljahrsschrift für gerichtliche Medizin und öffentliches Sanitätswesen. Berlin.

Vo.-med. Zh., Spb. Voenno-meditsinskii zhurnal. St. Petersburg.

Vo.-sanit. Dyelo. Voenno-sanitarnoe delo. Moskva.

Vrach, Spb. Vrach. St. Petersburg.

Vyestn. obshch. Gig., Spb. Vestnik obshchestvennoi gigieny, sudebnoi i prakticheskoi meditsiny. St. Petersburg.

Vyestn. Oftalm. Vestnik oftalmologii. Moskva.

*Vyestn. Vozd. Flota.** Vestnik Vozduschnago Flota. Moskva.

Vyestn. zhelyezn. Med. Vestnik zheleznodorozhnoi meditsiny i sanitarii. Saratov.

W. Va med. J. West Virginia Medical Journal. Wheeling.

*W. Va Univ. Bull.** West Virginia University Bulletin, Morgantown.

*War. Med., Chicago.** War Medicine. Chicago.

*Wash. Univ. med. Alum. Quart.** Washington University Medical Alumni Quarterly. St. Louis.

Wien. Klin. Wiener Klinik. Vorträge aus der gesammten praktischen Heilkunde. Wien.

Wien. klin. Rdsch. Wiener klinische Rundschau. Wien.

Wien. klin. Wschr. Wiener klinische Wochenschrift. Wien.

Wien. med. Pr. Wiener medizinische Presse. Wien.

Wien. med. Wschr. Wiener medizinische Wochenschrift. Wien.

Würzburg. Abh. prakt. Med. Würzburger Abhandlungen a. d. Gesamtgeb. der praktischen Medizin. Würzburg.

Yale J. Biol. Med. Yale Journal of Biology and Medicine. New Haven, Conn.

*Yale sci. Mag.** Yale Scientific Magazine. New Haven.

Z. ärztl. Fortbild. Zeitschrift für ärztliche Fortbildung. Jena.

Z. angew. Chem. Zeitschrift für angewandte Chemie und Zentralblatt für technische Chemie. Leipzig.

Z. Berg-, Hütt.-u. Salinenw. Zeitschrift für das Berg-, Hütten- u. Salinenwesen im Preussischen Staat. Berlin.

Z. Biol. Zeitschrift für Biologie. München.

Z. diätet. phys. Ther. Zeitschrift für diätetische und physikalische Therapie. Leipzig.

Z. Electrochem. Zeitschrift für Elektrochemie (u. angewandte physikalischer Chemie). Halle.

Z. exp. Path. Ther. Zeitschrift für experimentelle Pathologie und Therapie. Berlin.

Z. ges. exp. Med. Zeitschrift für die gesamte experimentelle Medizin. Berlin.

Z. ges. Neurol. Psychiat. Zeitschrift für die gesamte Neurologie und Psychiatrie. Berlin.

Z. ges. phys. Ther. Zeitschrift für die gesamte physikalische Therapie. Leipzig.

Z. GewHyg. Zeitschrift für Gewerbe-Hygiene und Unfallverhütung. Wien.

Z. Hals- Nas.- u. Ohrenheilk. Zeitschrift für Hals-, Nasen- und Ohrenheilkunde. Berlin.

Z. Hyg. InfektKr. Zeitschrift für Hygiene und Infektionskrankheiten. Berlin.

Z. klin. Med. Zeitschrift für klinische Medizin. Berlin.

Z. Krankenpfl. Zeitschrift für Krankenpflege und klinische Therapie. Berlin.

Z. Krebsforsch. Zeitschrift für Krebsforschung. Berlin.

Z. KreislForsch. Zeitschrift für Kreislaufforschung. Dresden.

Z. Laryng. Rhinol. Zeitschrift für Laryngologie, Rhinologie und ihre Grenzgebiete. Leipzig.

Z. MedBeamt. Zeitschrift für Medizinal-Beamte. Zentralblatt für gerichtliche Medizin, Hygiene, öffentl. Sanitätswesen und Medizinal-Gesetzgebung. Berlin.

Z. Ohrenheilk. Zeitschrift für Ohrenheilkunde. München.

Z. phys. Chem. Zeitschrift für Physikalische Chemie, Stöchiometrie und Verwandtschaftslehre. Leipzig.

*Z. rat. Med.** Zeitschrift für rationelle Medizin. Leipzig.

*Z. Ther. Einbzhung. Elect. Hydrother.** Zeitschrift für Therapie, mit Einbeziehung der Electro- und Hydrotherapie. Wien.

Zbl. allg. Path. path. Anat. Zentralblatt für allgemeine Pathologie und pathologischen Anatomie. Jena.

Zbl. Chir. Zentralblatt für Chirurgie. Leipzig.

Zbl. ges. Neurol. Psychiat. Zentralblatt für die gesamte Neurologie und Psychiatrie. Berlin.

Zbl. ges. Ophthal. Zentralblatt für die gesamte Ophthalmologie und ihri Grenzgebiete. Berlin.

Zbl. GewHyg. Zentralblatt für Gewerbehygiene und Unfallverhütung. Berlin.

Zbl. Gynäk. Zentralblatt für Gynäkologie. Leipzig.

Zbl. Hals-, Nas.- u. Ohrenheilk. Zentralblatt für Hals-, Nasen- und Ohrenheilkunde. Berlin.

Zbl. inn. Med. Zentralblatt für Innere Medizin. Leipzig.

*Zbl. klin. Med.** Zentralblatt für klinische Medicin. Bonn.

Zbl. med. Wiss. Zentralblatt für die medizinischen Wissenschaften. Berlin.

Zbl. Physiol. Zentralblatt für Physiologie. Leipzig; Wien.

Zbl. prakt. Augenheilk. Zentralblatt für praktische Augenheilkunde. Leipzig.

Zh. russk. Obshch. Okhran. nar. Zdray. Zhurnal Russkago obshchestva okhranenia narodnago zdravia. St. Petersburg.

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